

# SEQUENCE LISTING

<110> Lollar, John S.

<120> Nucleic Acid and Amino Acid Sequences  
encoding High-Level Expressor Factor VIII Polypeptides and  
Methods of Use

<130> 007157/ 276516

<150> PCT/US02/33403

<151> 2002-10-07

<150> 60/327,388

<151> 2001-10-05

<160> 21

<170> FastSEQ for Windows Version 4.0

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<211> 6402

<212> DNA

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<220>

<221> gene

<222> (1)...(6399)

<223> Factor VIII-- Full Length

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Glu	Asp	Asn	Ile	Met	Val	Thr	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr		
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Ser	Phe	Tyr	Ser	Ser	Leu	Ile	Ser	Tyr	Pro	Asp	Asp	Gln	Glu	Gln	Gly		
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gca	gaa	cct	cga	cac	aac	ttc	gtc	cag	cca	aat	gaa	acc	aga	act	tac	4848	
Ala	Glu	Pro	Arg	His	Asn	Phe	Val	Gln	Pro	Asn	Glu	Thr	Arg	Thr	Tyr		
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Phe	Trp	Lys	Val	Gln	His	His	Met	Ala	Pro	Thr	Glu	Asp	Glu	Phe	Asp		
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tgc	aaa	gcc	tgg	gcc	tac	ttt	tct	gat	gtt	gac	ctg	gaa	aaa	gat	gtg	4944	
Cys	Lys	Ala	Trp	Ala	Tyr	Phe	Ser	Asp	Val	Asp	Leu	Glu	Lys	Asp	Val		
		1635				1640						1645					
cac	tca	ggc	ttg	atc	ggc	ccc	ctt	ctg	atc	tgc	cgc	gcc	aac	acc	ctg	4992	
His	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Arg	Ala	Asn	Thr	Leu		
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aac	gct	gct	cac	ggg	aga	caa	gtg	acc	gtg	caa	gaa	ttt	gct	ctg	ttt	5040	
Asn	Ala	Ala	His	Gly	Arg	Gln	Val	Thr	Val	Gln	Glu	Phe	Ala	Leu	Phe		
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Phe	Thr	Ile	Phe	Asp	Glu	Thr	Lys	Ser	Trp	Tyr	Phe	Thr	Glu	Asn	Val		
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Glu	Arg	Asn	Cys	Arg	Ala	Pro	Cys	His	Leu	Gln	Met	Glu	Asp	Pro	Thr		
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ctg aaa gaa aac tat cgc ttc cat gca atc aat ggc tat gtg atg gat	5184
Leu Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Val Met Asp	
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Thr Leu Pro Gly Leu Val Met Ala Gln Asn Gln Arg Ile Arg Trp Tyr	
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ctg ctc agc atg ggc agc aat gaa aat atc cat tcg att cat ttt agc	5280
Leu Leu Ser Met Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser	
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gga cac gtg ttc agt gta cgg aaa aag gag gag tat aaa atg gcc gtg	5328
Gly His Val Phe Ser Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Val	
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tac aat ctc tat ccg ggt gtc ttt gag aca gtg gaa atg cta ccg tcc	5376
Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser	
1780 1785 1790	
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Lys Val Gly Ile Trp Arg Ile Glu Cys Leu Ile Gly Glu His Leu Gln	
1795 1800 1805	
gct ggg atg agc acg act ttc ctg gtg tac agc aag gag tgt cag gct	5472
Ala Gly Met Ser Thr Thr Phe Leu Val Tyr Ser Lys Glu Cys Gln Ala	
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Pro Leu Gly Met Ala Ser Gly Arg Ile Arg Asp Phe Gln Ile Thr Ala	
1825 1830 1835 1840	
tca gga cag tat gga cag tgg gcc cca aag ctg gcc aga ctt cat tat	5568
Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr	
1845 1850 1855	
tcc gga tca atc aat gcc tgg agc acc aag gat ccc cac tcc tgg atc	5616
Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Asp Pro His Ser Trp Ile	
1860 1865 1870	
aag gtg gat ctg ttg gca cca atg atc att cac ggc atc atg acc cag	5664
Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile Met Thr Gln	
1875 1880 1885	
ggt gcc cgt cag aag ttt tcc agc ctc tac atc tcc cag ttt atc atc	5712
Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile	
1890 1895 1900	
atg tac agt ctt gac ggg agg aac tgg cag agt tac cga ggg aat tcc	5760
Met Tyr Ser Leu Asp Gly Arg Asn Trp Gln Ser Tyr Arg Gly Asn Ser	
1905 1910 1915 1920	
acg ggc acc tta atg gtc ttc ttt ggc aat gtg gac gca tct ggg att	5808
Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ala Ser Gly Ile	
1925 1930 1935	
aaa cac aat att ttt aac cct ccg att gtg gct cgg tac atc cgt ttg	5856
Lys His Asn Ile Phe Asn Pro Pro Ile Val Ala Arg Tyr Ile Arg Leu	
1940 1945 1950	
cac cca aca cat tac agc atc cgc agc act ctt cgc atg gag ttg atg	5904
His Pro Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met	
1955 1960 1965	
ggc tgt gat tta aac agt tgc agc atg ccc ctg gga atg cag aat aaa	5952



Gly 1970	Cys	Asp	Leu	Asn	Ser	Cys 1975	Ser	Met	Pro	Leu	Gly 1980	Met	Gln	Asn	Lys	
gcg	ata	tca	gac	tca	cag	atc	acg	gcc	tcc	tcc	cac	cta	agc	aat	ata	6000
Ala	Ile	Ser	Asp	Ser	Gln	Ile	Thr	Ala	Ser	Ser	His	Leu	Ser	Asn	Ile	
1985					1990				1995						2000	
ttt	gcc	acc	tgg	tct	cct	tca	caa	gcc	cga	ctt	cac	ctc	cag	ggg	cgg	6048
Phe	Ala	Thr	Trp	Ser	Pro	Ser	Gln	Ala	Arg	Leu	His	Leu	Gln	Gly	Arg	
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acg	aat	gcc	tgg	cga	ccc	cgg	gtg	agc	agc	gca	gag	gag	tgg	ctg	cag	6096
Thr	Asn	Ala	Trp	Arg	Pro	Arg	Val	Ser	Ser	Ala	Glu	Glu	Trp	Leu	Gln	
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gtg	gac	ctg	cag	aag	acg	gtg	aag	gtc	aca	ggc	atc	acc	acc	cag	ggc	6144
Val	Asp	Leu	Gln	Lys	Thr	Val	Lys	Val	Thr	Gly	Ile	Thr	Thr	Gln	Gly	
		2035				2040						2045				
gtg	aag	tcc	ctg	ctc	agc	agc	atg	tat	gtg	aag	gag	ttc	ctc	gtg	tcc	6192
Val	Lys	Ser	Leu	Leu	Ser	Ser	Met	Tyr	Val	Lys	Glu	Phe	Leu	Val	Ser	
	2050				2055						2060					
agt	agt	cag	gac	ggc	cgc	cgc	tgg	acc	ctg	ttt	ctt	cag	gac	ggc	cac	6240
Ser	Ser	Gln	Asp	Gly	Arg	Arg	Trp	Thr	Leu	Phe	Leu	Gln	Asp	Gly	His	
2065					2070					2075					2080	
acg	aag	gtt	ttt	cag	ggc	aat	cag	gac	tcc	tcc	acc	ccc	gtg	gtg	aac	6288
Thr	Lys	Val	Phe	Gln	Gly	Asn	Gln	Asp	Ser	Ser	Thr	Pro	Val	Val	Asn	
				2085					2090					2095		
gct	ctg	gac	ccc	ccg	ctg	ttc	acg	cgc	tac	ctg	agg	atc	cac	ccc	acg	6336
Ala	Leu	Asp	Pro	Pro	Leu	Phe	Thr	Arg	Tyr	Leu	Arg	Ile	His	Pro	Thr	
			2100					2105					2110			
agc	tgg	gcg	cag	cac	atc	gcc	ctg	agg	ctc	gag	gtt	cta	gga	tgt	gag	6384
Ser	Trp	Ala	Gln	His	Ile	Ala	Leu	Arg	Leu	Glu	Val	Leu	Gly	Cys	Glu	
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gca	cag	gat	ctc	tac	tga											6402
Ala	Gln	Asp	Leu	Tyr												
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Gly	Phe	Ser	Ala	Ile	Arg	Arg	Tyr	Tyr	Leu	Gly	Ala	Val	Glu	Leu	Ser	
			20					25					30			
Trp	Asp	Tyr	Arg	Gln	Ser	Glu	Leu	Leu	Arg	Glu	Leu	His	Val	Asp	Thr	
		35					40					45				
Arg	Phe	Pro	Ala	Thr	Ala	Pro	Gly	Ala	Leu	Pro	Leu	Gly	Pro	Ser	Val	
		50				55					60					
Leu	Tyr	Lys	Lys	Thr	Val	Phe	Val	Glu	Phe	Thr	Asp	Gln	Leu	Phe	Ser	
65					70				75						80	
Val	Ala	Arg	Pro	Arg	Pro	Pro	Trp	Met	Gly	Leu	Leu	Gly	Pro	Thr	Ile	
				85					90					95		
Gln	Ala	Glu	Val	Tyr	Asp	Thr	Val	Val	Val	Thr	Leu	Lys	Asn	Met	Ala	
			100					105					110			
Ser	His	Pro	Val	Ser	Leu	His	Ala	Val	Gly	Val	Ser	Phe	Trp	Lys	Ser	
		115					120						125			

Ser	Glu	Gly	Ala	Glu	Tyr	Glu	Asp	His	Thr	Ser	Gln	Arg	Glu	Lys	Glu
130						135					140				
Asp	Asp	Lys	Val	Leu	Pro	Gly	Lys	Ser	Gln	Thr	Tyr	Val	Trp	Gln	Val
145					150					155					160
Leu	Lys	Glu	Asn	Gly	Pro	Thr	Ala	Ser	Asp	Pro	Pro	Cys	Leu	Thr	Tyr
				165					170					175	
Ser	Tyr	Leu	Ser	His	Val	Asp	Leu	Val	Lys	Asp	Leu	Asn	Ser	Gly	Leu
			180					185					190		
Ile	Gly	Ala	Leu	Leu	Val	Cys	Arg	Glu	Gly	Ser	Leu	Thr	Arg	Glu	Arg
	195					200						205			
Thr	Gln	Asn	Leu	His	Glu	Phe	Val	Leu	Leu	Phe	Ala	Val	Phe	Asp	Glu
	210					215						220			
Gly	Lys	Ser	Trp	His	Ser	Ala	Arg	Asn	Asp	Ser	Trp	Thr	Arg	Ala	Met
225					230					235					240
Asp	Pro	Ala	Pro	Ala	Arg	Ala	Gln	Pro	Ala	Met	His	Thr	Val	Asn	Gly
				245					250					255	
Tyr	Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Lys	Lys	Ser
		260						265					270		
Val	Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Ser	Pro	Glu	Val	His	Ser
	275					280						285			
Ile	Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	His	His	Arg	Gln	Ala
	290					295					300				
Ser	Leu	Glu	Ile	Ser	Pro	Leu	Thr	Phe	Leu	Thr	Ala	Gln	Thr	Phe	Leu
305					310					315					320
Met	Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	His
				325					330					335	
His	Gly	Gly	Met	Glu	Ala	His	Val	Arg	Val	Glu	Ser	Cys	Ala	Glu	Glu
			340					345					350		
Pro	Gln	Leu	Arg	Arg	Lys	Ala	Asp	Glu	Glu	Glu	Asp	Tyr	Asp	Asp	Asn
		355				360						365			
Leu	Tyr	Asp	Ser	Asp	Met	Asp	Val	Val	Arg	Leu	Asp	Gly	Asp	Asp	Val
	370					375					380				
Ser	Pro	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr
385					390					395					400
Trp	Val	His	Tyr	Ile	Ser	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro
				405					410					415	
Ala	Val	Pro	Ser	Pro	Ser	Asp	Arg	Ser	Tyr	Lys	Ser	Leu	Tyr	Leu	Asn
			420					425					430		
Ser	Gly	Pro	Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Ala	Arg	Phe	Val
	435					440						445			
Ala	Tyr	Thr	Asp	Val	Thr	Phe	Lys	Thr	Arg	Lys	Ala	Ile	Pro	Tyr	Glu
	450					455					460				
Ser	Gly	Ile	Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	Val	Gly	Asp	Thr	Leu
465					470				475						480
Leu	Ile	Ile	Phe	Lys	Asn	Lys	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro
				485					490					495	
His	Gly	Ile	Thr	Asp	Val	Ser	Ala	Leu	His	Pro	Gly	Arg	Leu	Leu	Lys
			500					505					510		
Gly	Trp	Lys	His	Leu	Lys	Asp	Met	Pro	Ile	Leu	Pro	Gly	Glu	Thr	Phe
		515				520						525			
Lys	Tyr	Lys	Trp	Thr	Val	Thr	Val	Glu	Asp	Gly	Pro	Thr	Lys	Ser	Asp
	530					535					540				
Pro	Arg	Cys	Leu	Thr	Arg	Tyr	Tyr	Ser	Ser	Ser	Ile	Asn	Leu	Glu	Lys
545					550					555					560
Asp	Leu	Ala	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Tyr	Lys	Glu
				565					570					575	
Ser	Val	Asp	Gln	Arg	Gly	Asn	Gln	Met	Met	Ser	Asp	Lys	Arg	Asn	Val
			580					585					590		
Ile	Leu	Phe	Ser	Val	Phe	Asp	Glu	Asn	Gln	Ser	Trp	Tyr	Leu	Ala	Glu
	595					600						605			
Asn	Ile	Gln	Arg	Phe	Leu	Pro	Asn	Pro	Asp	Gly	Leu	Gln	Pro	Gln	Asp
	610					615					620				
Pro	Glu	Phe	Gln	Ala	Ser	Asn	Ile	Met	His	Ser	Ile	Asn	Gly	Tyr	Val
625					630					635					640
Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp
				645					650					655	

Tyr	Ile	Leu	Ser	Val	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe
			660					665					670		
Ser	Gly	Tyr	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr
		675					680					685			
Leu	Phe	Pro	Phe	Ser	Gly	Glu	Thr	Val	Phe	Met	Ser	Met	Glu	Asn	Pro
		690				695					700				
Gly	Leu	Trp	Val	Leu	Gly	Cys	His	Asn	Ser	Asp	Leu	Arg	Asn	Arg	Gly
705					710					715					720
Met	Thr	Ala	Leu	Leu	Lys	Val	Tyr	Ser	Cys	Asp	Arg	Asp	Ile	Gly	Asp
			725						730					735	
Tyr	Tyr	Asp	Asn	Thr	Tyr	Glu	Asp	Ile	Pro	Gly	Phe	Leu	Leu	Ser	Gly
			740					745					750		
Lys	Asn	Val	Ile	Glu	Pro	Arg	Ser	Phe	Ala	Gln	Asn	Ser	Arg	Pro	Pro
		755					760					765			
Ser	Ala	Ser	Gln	Lys	Gln	Phe	Gln	Thr	Ile	Thr	Ser	Pro	Glu	Asp	Asp
		770				775					780				
Val	Glu	Leu	Asp	Pro	Gln	Ser	Gly	Glu	Arg	Thr	Gln	Ala	Leu	Glu	Glu
785					790					795					800
Leu	Ser	Val	Pro	Ser	Gly	Asp	Gly	Ser	Met	Leu	Leu	Gly	Gln	Asn	Pro
			805						810					815	
Ala	Pro	His	Gly	Ser	Ser	Ser	Ser	Asp	Leu	Gln	Glu	Ala	Arg	Asn	Glu
			820					825					830		
Ala	Asp	Asp	Tyr	Leu	Pro	Gly	Ala	Arg	Glu	Arg	Gly	Thr	Ala	Pro	Ser
		835				840						845			
Ala	Ala	Ala	Arg	Leu	Arg	Pro	Glu	Leu	His	His	Ser	Ala	Glu	Arg	Val
		850				855					860				
Leu	Thr	Pro	Glu	Pro	Glu	Lys	Glu	Leu	Lys	Lys	Leu	Asp	Ser	Lys	Met
865					870					875					880
Ser	Ser	Ser	Ser	Asp	Leu	Leu	Lys	Thr	Ser	Pro	Thr	Ile	Pro	Ser	Asp
			885						890					895	
Thr	Leu	Ser	Ala	Glu	Thr	Glu	Arg	Thr	His	Ser	Leu	Gly	Pro	Pro	His
			900					905					910		
Pro	Gln	Val	Asn	Phe	Arg	Ser	Gln	Leu	Gly	Ala	Ile	Val	Leu	Gly	Lys
		915					920					925			
Asn	Ser	Ser	His	Phe	Ile	Gly	Ala	Gly	Val	Pro	Leu	Gly	Ser	Thr	Glu
		930				935					940				
Glu	Asp	His	Glu	Ser	Ser	Leu	Gly	Glu	Asn	Val	Ser	Pro	Val	Glu	Ser
945					950					955					960
Asp	Gly	Ile	Phe	Glu	Lys	Glu	Arg	Ala	His	Gly	Pro	Ala	Ser	Leu	Thr
			965						970					975	
Lys	Asp	Asp	Val	Leu	Phe	Lys	Val	Asn	Ile	Ser	Leu	Val	Lys	Thr	Asn
		980						985					990		
Lys	Ala	Arg	Val	Tyr	Leu	Lys	Thr	Asn	Arg	Lys	Ile	His	Ile	Asp	Asp
		995					1000					1005			
Ala	Ala	Leu	Leu	Thr	Glu	Asn	Arg	Ala	Ser	Ala	Thr	Phe	Met	Asp	Lys
		1010				1015					1020				
Asn	Thr	Thr	Ala	Ser	Gly	Leu	Asn	His	Val	Ser	Asn	Trp	Ile	Lys	Gly
1025					1030					1035					1040
Pro	Leu	Gly	Lys	Asn	Pro	Leu	Ser	Ser	Glu	Arg	Gly	Pro	Ser	Pro	Glu
			1045						1050					1055	
Leu	Leu	Thr	Ser	Ser	Gly	Ser	Gly	Lys	Ser	Val	Lys	Gly	Gln	Ser	Ser
			1060					1065					1070		
Gly	Gln	Gly	Arg	Ile	Arg	Val	Ala	Val	Glu	Glu	Glu	Glu	Leu	Ser	Lys
		1075				1080						1085			
Gly	Lys	Glu	Met	Met	Leu	Pro	Asn	Ser	Glu	Leu	Thr	Phe	Leu	Thr	Asn
		1090				1095					1100				
Ser	Ala	Asp	Val	Gln	Gly	Asn	Asp	Thr	His	Ser	Gln	Gly	Lys	Lys	Ser
1105					1110					1115					1120
Arg	Glu	Glu	Met	Glu	Arg	Arg	Glu	Lys	Leu	Val	Gln	Glu	Lys	Val	Asp
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Leu	Pro	Gln	Val	Tyr	Thr	Ala	Thr	Gly	Thr	Lys	Asn	Phe	Leu	Arg	Asn
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Ile	Phe	His	Gln	Ser	Thr	Glu	Pro	Ser	Val	Glu	Gly	Phe	Asp	Gly	Gly
		1155				1160					1165				
Ser	His	Ala	Pro	Val	Pro	Gln	Asp	Ser	Arg	Ser	Leu	Asn	Asp	Ser	Ala
		1170				1175					1180				

Glu Arg Ala Glu Thr His Ile Ala His Phe Ser Ala Ile Arg Glu Glu	1185	1190	1195	1200
Ala Pro Leu Glu Ala Pro Gly Asn Arg Thr Gly Pro Gly Pro Arg Ser		1205	1210	1215
Ala Val Pro Arg Arg Val Lys Gln Ser Leu Lys Gln Ile Arg Leu Pro		1220	1225	1230
Leu Glu Glu Ile Lys Pro Glu Arg Gly Val Val Leu Asn Ala Thr Ser		1235	1240	1245
Thr Arg Trp Ser Glu Ser Ser Pro Ile Leu Gln Gly Ala Lys Arg Asn		1250	1255	1260
Asn Leu Ser Leu Pro Phe Leu Thr Leu Glu Met Ala Gly Gly Gln Gly		1265	1270	1275
Lys Ile Ser Ala Leu Gly Lys Ser Ala Ala Gly Pro Leu Ala Ser Gly		1285	1290	1295
Lys Leu Glu Lys Ala Val Leu Ser Ser Ala Gly Leu Ser Glu Ala Ser		1300	1305	1310
Gly Lys Ala Glu Phe Leu Pro Lys Val Arg Val His Arg Glu Asp Leu		1315	1320	1325
Leu Pro Gln Lys Thr Ser Asn Val Ser Cys Ala His Gly Asp Leu Gly		1330	1335	1340
Gln Glu Ile Phe Leu Gln Lys Thr Arg Gly Pro Val Asn Leu Asn Lys		1345	1350	1355
Val Asn Arg Pro Gly Arg Thr Pro Ser Lys Leu Leu Gly Pro Pro Met		1365	1370	1375
Pro Lys Glu Trp Glu Ser Leu Glu Lys Ser Pro Lys Ser Thr Ala Leu		1380	1385	1390
Arg Thr Lys Asp Ile Ile Ser Leu Pro Leu Asp Arg His Glu Ser Asn		1395	1400	1405
His Ser Ile Ala Ala Lys Asn Glu Gly Gln Ala Glu Thr Gln Arg Glu		1410	1415	1420
Ala Ala Trp Thr Lys Gln Gly Gly Pro Gly Arg Leu Cys Ala Pro Lys		1425	1430	1435
Pro Pro Val Leu Arg Arg His Gln Arg Asp Ile Ser Leu Pro Thr Phe		1445	1450	1455
Gln Pro Glu Glu Asp Lys Met Asp Tyr Asp Asp Ile Phe Ser Thr Glu		1460	1465	1470
Thr Lys Gly Glu Asp Phe Asp Ile Tyr Gly Glu Asp Glu Asn Gln Asp		1475	1480	1485
Pro Arg Ser Phe Gln Lys Arg Thr Arg His Tyr Phe Ile Ala Ala Val		1490	1495	1500
Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu Ser Pro Arg Ala Leu Arg		1505	1510	1515
Asn Arg Ala Gln Asn Gly Glu Val Pro Arg Phe Lys Lys Val Val Phe		1525	1530	1535
Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln Pro Ser Tyr Arg Gly Glu		1540	1545	1550
Leu Asn Lys His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val		1555	1560	1565
Glu Asp Asn Ile Met Val Thr Phe Lys Asn Gln Ala Ser Arg Pro Tyr		1570	1575	1580
Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro Asp Asp Gln Glu Gln Gly		1585	1590	1595
Ala Glu Pro Arg His Asn Phe Val Gln Pro Asn Glu Thr Arg Thr Tyr		1605	1610	1615
Phe Trp Lys Val Gln His His Met Ala Pro Thr Glu Asp Glu Phe Asp		1620	1625	1630
Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val		1635	1640	1645
His Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Arg Ala Asn Thr Leu		1650	1655	1660
Asn Ala Ala His Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe		1665	1670	1675
Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Val		1685	1690	1695
Glu Arg Asn Cys Arg Ala Pro Cys His Leu Gln Met Glu Asp Pro Thr		1700	1705	1710

Leu Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Val Met Asp  
 1715 1720 1725  
 Thr Leu Pro Gly Leu Val Met Ala Gln Asn Gln Arg Ile Arg Trp Tyr  
 1730 1735 1740  
 Leu Leu Ser Met Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser  
 1745 1750 1755 1760  
 Gly His Val Phe Ser Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Val  
 1765 1770 1775  
 Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser  
 1780 1785 1790  
 Lys Val Gly Ile Trp Arg Ile Glu Cys Leu Ile Gly Glu His Leu Gln  
 1795 1800 1805  
 Ala Gly Met Ser Thr Thr Phe Leu Val Tyr Ser Lys Glu Cys Gln Ala  
 1810 1815 1820  
 Pro Leu Gly Met Ala Ser Gly Arg Ile Arg Asp Phe Gln Ile Thr Ala  
 1825 1830 1835 1840  
 Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr  
 1845 1850 1855  
 Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Asp Pro His Ser Trp Ile  
 1860 1865 1870  
 Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile Met Thr Gln  
 1875 1880 1885  
 Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile  
 1890 1895 1900  
 Met Tyr Ser Leu Asp Gly Arg Asn Trp Gln Ser Tyr Arg Gly Asn Ser  
 1905 1910 1915 1920  
 Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ala Ser Gly Ile  
 1925 1930 1935  
 Lys His Asn Ile Phe Asn Pro Pro Ile Val Ala Arg Tyr Ile Arg Leu  
 1940 1945 1950  
 His Pro Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met  
 1955 1960 1965  
 Gly Cys Asp Leu Asn Ser Cys Ser Met Pro Leu Gly Met Gln Asn Lys  
 1970 1975 1980  
 Ala Ile Ser Asp Ser Gln Ile Thr Ala Ser Ser His Leu Ser Asn Ile  
 1985 1990 1995 2000  
 Phe Ala Thr Trp Ser Pro Ser Gln Ala Arg Leu His Leu Gln Gly Arg  
 2005 2010 2015  
 Thr Asn Ala Trp Arg Pro Arg Val Ser Ser Ala Glu Glu Trp Leu Gln  
 2020 2025 2030  
 Val Asp Leu Gln Lys Thr Val Lys Val Thr Gly Ile Thr Thr Gln Gly  
 2035 2040 2045  
 Val Lys Ser Leu Leu Ser Ser Met Tyr Val Lys Glu Phe Leu Val Ser  
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 Ser Ser Gln Asp Gly Arg Arg Trp Thr Leu Phe Leu Gln Asp Gly His  
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Gly	Phe	Ser	Ala	Ile	Arg	Arg	Tyr	Tyr	Leu	Gly	Ala	Val	Glu	Leu	Ser	
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tgg	gac	tac	cgg	caa	agt	gaa	ctc	ctc	cgt	gag	ctg	cac	gtg	gac	acc	144
Trp	Asp	Tyr	Arg	Gln	Ser	Glu	Leu	Leu	Arg	Glu	Leu	His	Val	Asp	Thr	
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aga	ttt	cct	gct	aca	gcg	cca	gga	gct	ctt	ccg	ttg	ggc	ccg	tca	gtc	192
Arg	Phe	Pro	Ala	Thr	Ala	Pro	Gly	Ala	Leu	Pro	Leu	Gly	Pro	Ser	Val	
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ctg	tac	aaa	aag	act	gtg	ttc	gta	gag	ttc	acg	gat	caa	ctt	ttc	agc	240
Leu	Tyr	Lys	Lys	Thr	Val	Phe	Val	Glu	Phe	Thr	Asp	Gln	Leu	Phe	Ser	
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Val	Ala	Arg	Pro	Arg	Pro	Pro	Trp	Met	Gly	Leu	Leu	Gly	Pro	Thr	Ile	
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cag	gct	gag	gtt	tac	gac	acg	gtg	gtc	gtt	acc	ctg	aag	aac	atg	gct	336
Gln	Ala	Glu	Val	Tyr	Asp	Thr	Val	Val	Val	Thr	Leu	Lys	Asn	Met	Ala	
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Ser	His	Pro	Val	Ser	Leu	His	Ala	Val	Gly	Val	Ser	Phe	Trp	Lys	Ser	
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Ser	Glu	Gly	Ala	Glu	Tyr	Glu	Asp	His	Thr	Ser	Gln	Arg	Glu	Lys	Glu	
	130					135					140					
gac	gat	aaa	gtc	ctt	ccc	ggg	aaa	agc	caa	acc	tac	gtc	tgg	cag	gtc	480
Asp	Asp	Lys	Val	Leu	Pro	Gly	Lys	Ser	Gln	Thr	Tyr	Val	Trp	Gln	Val	
145					150				155					160		
ctg	aaa	gaa	aat	ggg	cca	aca	gcc	tct	gac	cca	cca	tgt	ctt	acc	tac	528
Leu	Lys	Glu	Asn	Gly	Pro	Thr	Ala	Ser	Asp	Pro	Pro	Cys	Leu	Thr	Tyr	
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tca	tac	ctg	tct	cac	gtg	gac	ctg	gtg	aaa	gac	ctg	aat	tcg	ggc	ctc	576
Ser	Tyr	Leu	Ser	His	Val	Asp	Leu	Val	Lys	Asp	Leu	Asn	Ser	Gly	Leu	
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Ile	Gly	Ala	Leu	Leu	Val	Cys	Arg	Glu	Gly	Ser	Leu	Thr	Arg	Glu	Arg	
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acc	cag	aac	ctg	cac	gaa	ttt	gta	cta	ctt	ttt	gct	gtc	ttt	gat	gaa	672
Thr	Gln	Asn	Leu	His	Glu	Phe	Val	Leu	Leu	Phe	Ala	Val	Phe	Asp	Glu	
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Gly	Lys	Ser	Trp	His	Ser	Ala	Arg	Asn	Asp	Ser	Trp	Thr	Arg	Ala	Met	
225					230				235					240		
gat	ccc	gca	cct	gcc	agg	gcc	cag	cct	gca	atg	cac	aca	gtc	aat	ggc	768
Asp	Pro	Ala	Pro	Ala	Arg	Ala	Gln	Pro	Ala	Met	His	Thr	Val	Asn	Gly	

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Tyr	Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Lys	Lys	Ser															
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Val	Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Ser	Pro	Glu	Val	His	Ser															
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Ile	Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	His	His	Arg	Gln	Ala															
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Met	Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	His															
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His	Gly	Gly	Met	Glu	Ala	His	Val	Arg	Val	Glu	Ser	Cys	Ala	Glu	Glu															
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Pro	Gln	Leu	Arg	Arg	Lys	Ala	Asp	Glu	Glu	Glu	Asp	Tyr	Asp	Asp	Asn															
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Ser	Pro	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr															
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Trp	Val	His	Tyr	Ile	Ser	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro															
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gcg	gtc	ccc	agc	ccc	agt	gac	aga	agt	tat	aaa	agt	ctc	tac	ttg	aac	1296														
Ala	Val	Pro	Ser	Pro	Ser	Asp	Arg	Ser	Tyr	Lys	Ser	Leu	Tyr	Leu	Asn															
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agt	ggg	cct	cag	cga	att	ggg	agg	aaa	tac	aaa	aaa	gct	cga	ttc	gtc	1344														
Ser	Gly	Pro	Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Ala	Arg	Phe	Val															
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Ala	Tyr	Thr	Asp	Val	Thr	Phe	Lys	Thr	Arg	Lys	Ala	Ile	Pro	Tyr	Glu															
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Leu	Ile	Ile	Phe	Lys	Asn	Lys	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro															
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cat	gga	atc	act	gat	gtc	agc	gct	ttg	cac	cca	ggg	aga	ctt	cta	aaa	1536														
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Gly Trp Lys His Leu Lys Asp Met Pro Ile Leu Pro Gly Glu Thr Phe	
515 520 525	
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Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp	
530 535 540	
cct cgg tgc ctg acc cgc tac tac tcg agc tcc att aat cta gag aaa	1680
Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Ser Ile Asn Leu Glu Lys	
545 550 555 560	
gat ctg gct tcg gga ctc att ggc cct ctc ctc atc tgc tac aaa gaa	1728
Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu	
565 570 575	
tct gta gac caa aga gga aac cag atg atg tca gac aag aga aac gtc	1776
Ser Val Asp Gln Arg Gly Asn Gln Met Met Ser Asp Lys Arg Asn Val	
580 585 590	
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Ile Leu Phe Ser Val Phe Asp Glu Asn Gln Ser Trp Tyr Leu Ala Glu	
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aat att cag cgc ttc ctc ccc aat ccg gat gga tta cag ccc cag gat	1872
Asn Ile Gln Arg Phe Leu Pro Asn Pro Asp Gly Leu Gln Pro Gln Asp	
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Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val	
625 630 635 640	
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Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp	
645 650 655	
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Tyr Ile Leu Ser Val Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe	
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Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr	
675 680 685	
ctg ttc ccc ttc tca gga gaa acg gtc ttc atg tca atg gaa aac cca	2112
Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro	
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705 710 715 720	
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Met Thr Ala Leu Leu Lys Val Tyr Ser Cys Asp Arg Asp Ile Gly Asp	
725 730 735	
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Tyr Tyr Asp Asn Thr Tyr Glu Asp Ile Pro Gly Phe Leu Leu Ser Gly	
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Lys Asn Val Ile Glu Pro Arg Ser Phe Ala Gln Asn Ser Arg Pro Pro	
755 760 765	
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Ser Ala Ser Ala Pro Lys Pro Pro Val Leu Arg Arg His Gln Arg Asp	



770	775	780	
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cag gcg tct cgt ccc tat tcc ttc tac tcg agc ctt att tct tat ccg Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro 915 920 925	2784		
gat gat cag gag caa ggg gca gaa cct cga cac aac ttc gtc cag cca Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn Phe Val Gln Pro 930 935 940	2832		
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Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu	
1125 1130 1135	
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Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr	
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Ser Lys Glu Cys Gln Ala Pro Leu Gly Met Ala Ser Gly Arg Ile Arg	
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Asp Pro His Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile	
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Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Arg Asn Trp Gln	
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 Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser  
 20 25 30  
 Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr  
 35 40 45  
 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val  
 50 55 60  
 Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser  
 65 70 75 80  
 Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile  
 85 90 95  
 Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala  
 100 105 110  
 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser  
 115 120 125  
 Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu

130	135	140
Asp Asp Lys Val Leu	Pro Gly Lys Ser Gln Thr	Tyr Val Trp Gln Val
145	150	155
Leu Lys Glu Asn Gly	Pro Thr Ala Ser Asp	Pro Pro Cys Leu Thr Tyr
165	170	175
Ser Tyr Leu Ser His	Val Asp Leu Val Lys	Asp Leu Asn Ser Gly Leu
180	185	190
Ile Gly Ala Leu Leu	Val Cys Arg Glu Gly	Ser Leu Thr Arg Glu Arg
195	200	205
Thr Gln Asn Leu His	Glu Phe Val Leu Leu	Phe Ala Val Phe Asp Glu
210	215	220
Gly Lys Ser Trp His	Ser Ala Arg Asn Asp	Ser Trp Thr Arg Ala Met
225	230	235
Asp Pro Ala Pro Ala	Arg Ala Gln Pro Ala	Met His Thr Val Asn Gly
245	250	255
Tyr Val Asn Arg Ser	Leu Pro Gly Leu Ile	Gly Cys His Lys Lys Ser
260	265	270
Val Tyr Trp His Val	Ile Gly Met Gly Thr	Ser Pro Glu Val His Ser
275	280	285
Ile Phe Leu Glu Gly	His Thr Phe Leu Val	Arg His His Arg Gln Ala
290	295	300
Ser Leu Glu Ile Ser	Pro Leu Thr Phe Leu	Thr Ala Gln Thr Phe Leu
305	310	315
Met Asp Leu Gly Gln	Phe Leu Leu Phe Cys	His Ile Ser Ser His His
325	330	335
His Gly Gly Met Glu	Ala His Val Arg Val	Glu Ser Cys Ala Glu Glu
340	345	350
Pro Gln Leu Arg Arg	Lys Ala Asp Glu Glu	Asp Tyr Asp Asp Asn
355	360	365
Leu Tyr Asp Ser Asp	Met Asp Val Val Arg	Leu Asp Gly Asp Asp Val
370	375	380
Ser Pro Phe Ile Gln	Ile Arg Ser Val Ala	Lys Lys His Pro Lys Thr
385	390	395
Trp Val His Tyr Ile	Ser Ala Glu Glu Glu	Asp Trp Asp Tyr Ala Pro
405	410	415
Ala Val Pro Ser Pro	Ser Asp Arg Ser Tyr	Lys Ser Leu Tyr Leu Asn
420	425	430
Ser Gly Pro Gln Arg	Ile Gly Arg Lys Tyr	Lys Lys Ala Arg Phe Val
435	440	445
Ala Tyr Thr Asp Val	Thr Phe Lys Thr Arg	Lys Ala Ile Pro Tyr Glu
450	455	460
Ser Gly Ile Leu Gly	Pro Leu Leu Tyr Gly	Glu Val Gly Asp Thr Leu
465	470	475
Leu Ile Ile Phe Lys	Asn Lys Ala Ser Arg	Pro Tyr Asn Ile Tyr Pro
485	490	495
His Gly Ile Thr Asp	Val Ser Ala Leu His	Pro Gly Arg Leu Leu Lys
500	505	510
Gly Trp Lys His Leu	Lys Asp Met Pro Ile	Leu Pro Gly Glu Thr Phe
515	520	525
Lys Tyr Lys Trp Thr	Val Thr Val Glu Asp	Gly Pro Thr Lys Ser Asp
530	535	540
Pro Arg Cys Leu Thr	Arg Tyr Tyr Ser Ser	Ser Ile Asn Leu Glu Lys
545	550	555
Asp Leu Ala Ser Gly	Leu Ile Gly Pro Leu	Leu Ile Cys Tyr Lys Glu
565	570	575
Ser Val Asp Gln Arg	Gly Asn Gln Met Met	Ser Asp Lys Arg Asn Val
580	585	590
Ile Leu Phe Ser Val	Phe Asp Glu Asn Gln	Ser Trp Tyr Leu Ala Glu
595	600	605
Asn Ile Gln Arg Phe	Leu Pro Asn Pro Asp	Gly Leu Gln Pro Gln Asp
610	615	620
Pro Glu Phe Gln Ala	Ser Asn Ile Met His	Ser Ile Asn Gly Tyr Val
625	630	635
Phe Asp Ser Leu Gln	Leu Ser Val Cys Leu	His Glu Val Ala Tyr Trp
645	650	655
Tyr Ile Leu Ser Val	Gly Ala Gln Thr Asp	Phe Leu Ser Val Phe Phe



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1185          1190          1195          1200
Asp Pro His Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile
          1205          1210          1215
His Gly Ile Met Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr
          1220          1225          1230
Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Arg Asn Trp Gln
          1235          1240          1245
Ser Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn
          1250          1255          1260
Val Asp Ala Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Val
1265          1270          1275          1280
Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr
          1285          1290          1295
Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro
          1300          1305          1310
Leu Gly Met Gln Asn Lys Ala Ile Ser Asp Ser Gln Ile Thr Ala Ser
          1315          1320          1325
Ser His Leu Ser Asn Ile Phe Ala Thr Trp Ser Pro Ser Gln Ala Arg
          1330          1335          1340
Leu His Leu Gln Gly Arg Thr Asn Ala Trp Arg Pro Arg Val Ser Ser
1345          1350          1355          1360
Ala Glu Glu Trp Leu Gln Val Asp Leu Gln Lys Thr Val Lys Val Thr
          1365          1370          1375
Gly Ile Thr Thr Gln Gly Val Lys Ser Leu Leu Ser Ser Met Tyr Val
          1380          1385          1390
Lys Glu Phe Leu Val Ser Ser Ser Gln Asp Gly Arg Arg Trp Thr Leu
          1395          1400          1405
Phe Leu Gln Asp Gly His Thr Lys Val Phe Gln Gly Asn Gln Asp Ser
          1410          1415          1420
Ser Thr Pro Val Val Asn Ala Leu Asp Pro Pro Leu Phe Thr Arg Tyr
1425          1430          1435          1440
Leu Arg Ile His Pro Thr Ser Trp Ala Gln His Ile Ala Leu Arg Leu
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Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr
          1460          1465

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<210> 5
<211> 9009
<212> DNA
<213> Homo sapiens

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<220>
<221> gene
<222> (0)...(0)
<223> Factor VIII- Full Length

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<221> CDS
<222> (208)...(7203)

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tctccagttg aacatttgta gcaataagtc atgcaaatag agctctccac ctgcttcttt 180
ctgtgccttt tgcgattctg ctttagt gcc acc aga aga tac tac ctg ggt gca 234
Ala Thr Arg Arg Tyr Tyr Leu Gly Ala
          1          5

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gtg gaa ctg tca tgg gac tat atg caa agt gat ctc ggt gag ctg cct 282
Val Glu Leu Ser Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro
  10          15          20          25

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gtg gac gca aga ttt cct cct aga gtg cca aaa tct ttt cca ttc aac 330
Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn
          30          35          40

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acc tca gtc gtg tac aaa aag act ctg ttt gta gaa ttc acg gtt cac	378
Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Val His	
45 50 55	
ctt ttc aac atc gct aag cca agg cca ccc tgg atg ggt ctg cta ggt	426
Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly	
60 65 70	
cct acc atc cag gct gag gtt tat gat aca gtg gtc att aca ctt aag	474
Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys	
75 80 85	
aac atg gct tcc cat cct gtc agt ctt cat gct gtt ggt gta tcc tac	522
Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr	
90 95 100 105	
tgg aaa gct tct gag gga gct gaa tat gat gat cag acc agt caa agg	570
Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg	
110 115 120	
gag aaa gaa gat gat aaa gtc ttc cct ggt gga agc cat aca tat gtc	618
Glu Lys Glu Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val	
125 130 135	
tgg cag gtc ctg aaa gag aat ggt cca atg gcc tct gac cca ctg tgc	666
Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys	
140 145 150	
ctt acc tac tca tat ctt tct cat gtg gac ctg gta aaa gac ttg aat	714
Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn	
155 160 165	
tca ggc ctc att gga gcc cta cta gta tgt aga gaa ggg agt ctg gcc	762
Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala	
170 175 180 185	
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Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val	
190 195 200	
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Phe Asp Glu Gly Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met	
205 210 215	
cag gat agg gat gct gca tct gct cgg gcc tgg cct aaa atg cac aca	906
Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr	
220 225 230	
gtc aat ggt tat gta aac agg tct ctg cca ggt ctg att gga tgc cac	954
Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His	
235 240 245	
agg aaa tca gtc tat tgg cat gtg att gga atg ggc acc act cct gaa	1002
Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu	
250 255 260 265	
gtg cac tca ata ttc ctc gaa ggt cac aca ttt ctt gtg agg aac cat	1050
Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His	
270 275 280	
cgc cag gcg tcc ttg gaa atc tcg cca ata act ttc ctt act gct caa	1098
Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln	
285 290 295	
aca ctc ttg atg gac ctt gga cag ttt cta ctg ttt tgt cat atc tct	1146
Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser	

300	305	310	
tcc cac caa cat gat ggc atg gaa gct tat gtc aaa gta gac agc tgt Ser His Gln His Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys 315 320 325			1194
cca gag gaa ccc caa cta cga atg aaa aat aat gaa gaa gcg gaa gac Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp 330 335 340 345			1242
tat gat gat gat ctt act gat tct gaa atg gat gtg gtc agg ttt gat Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp 350 355 360			1290
gat gac aac tct cct tcc ttt atc caa att cgc tca gtt gcc aag aag Asp Asp Asn Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys 365 370 375			1338
cat cct aaa act tgg gta cat tac att gct gct gaa gag gag gac tgg His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp 380 385 390			1386
gac tat gct ccc tta gtc ctc gcc ccc gat gac aga agt tat aaa agt Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser 395 400 405			1434
caa tat ttg aac aat ggc cct cag cgg att ggt agg aag tac aaa aaa Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys 410 415 420 425			1482
gtc cga ttt atg gca tac aca gat gaa acc ttt aag act cgt gaa gct Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala 430 435 440			1530
att cag cat gaa tca gga atc ttg gga cct tta ctt tat ggg gaa gtt Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val 445 450 455			1578
gga gac aca ctg ttg att ata ttt aag aat caa gca agc aga cca tat Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr 460 465 470			1626
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gga gaa ata ttc aaa tat aaa tgg aca gtg act gta gaa gat ggg cca Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro 510 515 520			1770
act aaa tca gat cct cgg tgc ctg acc cgc tat tac tct agt ttc gtt Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val 525 530 535			1818
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tgc tac aaa gaa tct gta gat caa aga gga aac cag ata atg tca gac Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp 555 560 565			1914



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Lys	Arg	Asn	Val	Ile	Leu	Phe	Ser	Val	Phe	Asp	Glu	Asn	Arg	Ser	Trp	
570					575					580					585	
tac	ctc	aca	gag	aat	ata	caa	cgc	ttt	ctc	ccc	aat	cca	gct	gga	gtg	2010
Tyr	Leu	Thr	Glu	Asn	Ile	Gln	Arg	Phe	Leu	Pro	Asn	Pro	Ala	Gly	Val	
				590					595					600		
cag	ctt	gag	gat	cca	gag	ttc	caa	gcc	tcc	aac	atc	atg	cac	agc	atc	2058
Gln	Leu	Glu	Asp	Pro	Glu	Phe	Gln	Ala	Ser	Asn	Ile	Met	His	Ser	Ile	
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aat	ggc	tat	gtt	ttt	gat	agt	ttg	cag	ttg	tca	gtt	tgt	ttg	cat	gag	2106
Asn	Gly	Tyr	Val	Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	
	620						625					630				
gtg	gca	tac	tgg	tac	att	cta	agc	att	gga	gca	cag	act	gac	ttc	ctt	2154
Val	Ala	Tyr	Trp	Tyr	Ile	Leu	Ser	Ile	Gly	Ala	Gln	Thr	Asp	Phe	Leu	
	635					640					645					
tct	gtc	ttc	ttc	tct	gga	tat	acc	ttc	aaa	cac	aaa	atg	gtc	tat	gaa	2202
Ser	Val	Phe	Phe	Ser	Gly	Tyr	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	
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gac	aca	ctc	acc	cta	ttc	cca	ttc	tca	gga	gaa	act	gtc	ttc	atg	tcg	2250
Asp	Thr	Leu	Thr	Leu	Phe	Pro	Phe	Ser	Gly	Glu	Thr	Val	Phe	Met	Ser	
				670					675					680		
atg	gaa	aac	cca	ggg	cta	tgg	att	ctg	ggg	tgc	cac	aac	tca	gac	ttt	2298
Met	Glu	Asn	Pro	Gly	Leu	Trp	Ile	Leu	Gly	Cys	His	Asn	Ser	Asp	Phe	
			685					690					695			
cgg	aac	aga	ggc	atg	acc	gcc	tta	ctg	aag	gtt	tct	agt	tgt	gac	aag	2346
Arg	Asn	Arg	Gly	Met	Thr	Ala	Leu	Leu	Lys	Val	Ser	Ser	Cys	Asp	Lys	
	700					705					710					
aac	act	ggg	gat	tat	tac	gag	gac	agt	tat	gaa	gat	att	tca	gca	tac	2394
Asn	Thr	Gly	Asp	Tyr	Tyr	Glu	Asp	Ser	Tyr	Glu	Asp	Ile	Ser	Ala	Tyr	
	715					720					725					
ttg	ctg	agt	aaa	aac	aat	gcc	att	gaa	cca	aga	agc	ttc	tcc	cag	aat	2442
Leu	Leu	Ser	Lys	Asn	Asn	Ala	Ile	Glu	Pro	Arg	Ser	Phe	Ser	Gln	Asn	
730					735					740					745	
tca	aga	cac	cct	agc	act	agg	caa	aag	caa	ttt	aat	gcc	acc	aca	att	2490
Ser	Arg	His	Pro	Ser	Thr	Arg	Gln	Lys	Gln	Phe	Asn	Ala	Thr	Thr	Ile	
				750					755					760		
cca	gaa	aat	gac	ata	gag	aag	act	gac	cct	tgg	ttt	gca	cac	aga	aca	2538
Pro	Glu	Asn	Asp	Ile	Glu	Lys	Thr	Asp	Pro	Trp	Phe	Ala	His	Arg	Thr	
			765					770				775				
cct	atg	cct	aaa	ata	caa	aat	gtc	tcc	tct	agt	gat	ttg	ttg	atg	ctc	2586
Pro	Met	Pro	Lys	Ile	Gln	Asn	Val	Ser	Ser	Ser	Asp	Leu	Leu	Met	Leu	
		780					785					790				
ttg	cga	cag	agt	cct	act	cca	cat	ggg	cta	tcc	tta	tct	gat	ctc	caa	2634
Leu	Arg	Gln	Ser	Pro	Thr	Pro	His	Gly	Leu	Ser	Leu	Ser	Asp	Leu	Gln	
	795					800					805					
gaa	gcc	aaa	tat	gag	act	ttt	tct	gat	gat	cca	tca	cct	gga	gca	ata	2682
Glu	Ala	Lys	Tyr	Glu	Thr	Phe	Ser	Asp	Asp	Pro	Ser	Pro	Gly	Ala	Ile	
810					815					820					825	
gac	agt	aat	aac	agc	ctg	tct	gaa	atg	aca	cac	ttc	agg	cca	cag	ctc	2730
Asp	Ser	Asn	Asn	Ser	Leu	Ser	Glu	Met	Thr	His	Phe	Arg	Pro	Gln	Leu	

26

aag atg cta ttc ttg cca gaa tca gca agg tgg ata caa agg act cat	3546
Lys Met Leu Phe Leu Pro Glu Ser Ala Arg Trp Ile Gln Arg Thr His	
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1115 1120 1125	
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Glu Lys Asn Lys Val Val Val Gly Lys Gly Glu Phe Thr Lys Asp Val	
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1195 1200 1205	
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Thr Asn Arg Thr Lys Lys His Thr Ala His Phe Ser Lys Lys Gly Glu	
1260 1265 1270	
gaa gaa aac ttg gaa ggc ttg gga aat caa acc aag caa att gta gag	4074
Glu Glu Asn Leu Glu Gly Leu Gly Asn Gln Thr Lys Gln Ile Val Glu	
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aaa tat gca tgc acc aca agg ata tct cct aat aca agc cag cag aat	4122
Lys Tyr Ala Cys Thr Thr Arg Ile Ser Pro Asn Thr Ser Gln Gln Asn	
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Phe Val Thr Gln Arg Ser Lys Arg Ala Leu Lys Gln Phe Arg Leu Pro	
1310 1315 1320	
cta gaa gaa aca gaa ctt gaa aaa agg ata att gtg gat gac acc tca	4218
Leu Glu Glu Thr Glu Leu Glu Lys Arg Ile Ile Val Asp Asp Thr Ser	
1325 1330 1335	
acc cag tgg tcc aaa aac atg aaa cat ttg acc ccg agc acc ctc aca	4266
Thr Gln Trp Ser Lys Asn Met Lys His Leu Thr Pro Ser Thr Leu Thr	
1340 1345 1350	
cag ata gac tac aat gag aag gag aaa ggg gcc att act cag tct ccc	4314
Gln Ile Asp Tyr Asn Glu Lys Glu Lys Gly Ala Ile Thr Gln Ser Pro	

1355	1360	1365	
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tct cca tta ccc att gca aag gta tca tca ttt cca tct att aga cct Ser Pro Leu Pro Ile Ala Lys Val Ser Ser Phe Pro Ser Ile Arg Pro 1390 1395 1400			4410
ata tat ctg acc agg gtc cta ttc caa gac aac tct tct cat ctt cca Ile Tyr Leu Thr Arg Val Leu Phe Gln Asp Asn Ser Ser His Leu Pro 1405 1410 1415			4458
gca gca tct tat aga aag aaa gat tct ggg gtc caa gaa agc agt cat Ala Ala Ser Tyr Arg Lys Lys Asp Ser Gly Val Gln Glu Ser Ser His 1420 1425 1430			4506
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gcc aca aat tca gtc aca tac aag aaa gtt gag aac act gtt ctc ccg Ala Thr Asn Ser Val Thr Tyr Lys Lys Val Glu Asn Thr Val Leu Pro 1470 1475 1480			4650
aaa cca gac ttg ccc aaa aca tct ggc aaa gtt gaa ttg ctt cca aaa Lys Pro Asp Leu Pro Lys Thr Ser Gly Lys Val Glu Leu Leu Pro Lys 1485 1490 1495			4698
gtt cac att tat cag aag gac cta ttc cct acg gaa act agc aat ggg Val His Ile Tyr Gln Lys Asp Leu Phe Pro Thr Glu Thr Ser Asn Gly 1500 1505 1510			4746
tct cct ggc cat ctg gat ctc gtg gaa ggg agc ctt ctt cag gga aca Ser Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu Leu Gln Gly Thr 1515 1520 1525			4794
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gaa gag tgg aaa tcc caa gag aag tca cca gaa aaa aca gct ttt aag Glu Glu Trp Lys Ser Gln Glu Lys Ser Pro Glu Lys Thr Ala Phe Lys 1580 1585 1590			4986
aaa aag gat acc att ttg tcc ctg aac gct tgt gaa agc aat cat gca Lys Lys Asp Thr Ile Leu Ser Leu Asn Ala Cys Glu Ser Asn His Ala 1595 1600 1605			5034
ata gca gca ata aat gag gga caa aat aag ccc gaa ata gaa gtc acc Ile Ala Ala Ile Asn Glu Gly Gln Asn Lys Pro Glu Ile Glu Val Thr 1610 1615 1620 1625			5082

tgg gca aag caa ggt agg act gaa agg ctg tgc tct caa aac cca cca	5130
Trp Ala Lys Gln Gly Arg Thr Glu Arg Leu Cys Ser Gln Asn Pro Pro	
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gtc ttg aaa cgc cat caa cgg gaa ata act cgt act act ctt cag tca	5178
Val Leu Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser	
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gat caa gag gaa att gac tat gat gat acc ata tca gtt gaa atg aag	5226
Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys	
1660 1665 1670	
aag gaa gat ttt gac att tat gat gag gat gaa aat cag agc ccc cgc	5274
Lys Glu Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg	
1675 1680 1685	
agc ttt caa aag aaa aca cga cac tat ttt att gct gca gtg gag agg	5322
Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg	
1690 1695 1700 1705	
ctc tgg gat tat ggg atg agt agc tcc cca cat gtt cta aga aac agg	5370
Leu Trp Asp Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg	
1710 1715 1720	
gct cag agt ggc agt gtc cct cag ttc aag aaa gtt gtt ttc cag gaa	5418
Ala Gln Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu	
1725 1730 1735	
ttt act gat ggc tcc ttt act cag ccc tta tac cgt gga gaa cta aat	5466
Phe Thr Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn	
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Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp	
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Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe	
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tat tct agc ctt att tct tat gag gaa gat cag agg caa gga gca gaa	5610
Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu	
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cct aga aaa aac ttt gtc aag cct aat gaa acc aaa act tac ttt tgg	5658
Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp	
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Lys Val Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys	
1820 1825 1830	
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Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser	
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Gly Leu Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro	
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Ala His Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr	
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Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg	

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Asn	Cys	Arg	Ala	Pro	Cys	Asn	Ile	Gln	Met	Glu	Asp	Pro	Thr	Phe	Lys	
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Glu	Asn	Tyr	Arg	Phe	His	Ala	Ile	Asn	Gly	Tyr	Ile	Met	Asp	Thr	Leu	
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cct	ggc	tta	gta	atg	gct	cag	gat	caa	agg	att	cga	tgg	tat	ctg	ctc	6042
Pro	Gly	Leu	Val	Met	Gln	Ala	Asp	Gln	Arg	Ile	Arg	Trp	Tyr	Leu	Leu	
1930					1935					1940					1945	
agc	atg	ggc	agc	aat	gaa	aac	atc	cat	tct	att	cat	ttc	agt	gga	cat	6090
Ser	Met	Gly	Ser	Asn	Glu	Asn	Ile	His	Ser	Ile	His	Phe	Ser	Gly	His	
1950					1955					1960						
gtg	ttc	act	gta	cga	aaa	aaa	gag	gag	tat	aaa	atg	gca	ctg	tac	aat	6138
Val	Phe	Thr	Val	Arg	Lys	Lys	Glu	Glu	Tyr	Lys	Met	Ala	Leu	Tyr	Asn	
1965					1970					1975						
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Leu	Tyr	Pro	Gly	Val	Phe	Glu	Thr	Val	Glu	Met	Leu	Pro	Ser	Lys	Ala	
1980					1985					1990						
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Gly	Ile	Trp	Arg	Val	Glu	Cys	Leu	Ile	Gly	Glu	His	Leu	His	Ala	Gly	
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atg	agc	aca	ctt	ttt	ctg	gtg	tac	agc	aat	aag	tgt	cag	act	ccc	ctg	6282
Met	Ser	Thr	Leu	Phe	Leu	Val	Tyr	Ser	Asn	Lys	Cys	Gln	Thr	Pro	Leu	
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Gly	Met	Ala	Ser	Gly	His	Ile	Arg	Asp	Phe	Gln	Ile	Thr	Ala	Ser	Gly	
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caa	tat	gga	cag	tgg	gcc	cca	aag	ctg	gcc	aga	ctt	cat	tat	tcc	gga	6378
Gln	Tyr	Gly	Gln	Trp	Ala	Pro	Lys	Leu	Ala	Arg	Leu	His	Tyr	Ser	Gly	
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Ser	Ile	Asn	Ala	Trp	Ser	Thr	Lys	Glu	Pro	Phe	Ser	Trp	Ile	Lys	Val	
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Asp	Leu	Leu	Ala	Pro	Met	Ile	Ile	His	Gly	Ile	Lys	Thr	Gln	Gly	Ala	
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cgt	cag	aag	ttc	tcc	agc	ctc	tac	atc	tct	cag	ttt	atc	atc	atg	tat	6522
Arg	Gln	Lys	Phe	Ser	Ser	Leu	Tyr	Ile	Ser	Gln	Phe	Ile	Ile	Met	Tyr	
2090					2095					2100					2105	
agt	ctt	gat	ggg	aag	aag	tgg	cag	act	tat	cga	gga	aat	tcc	act	gga	6570
Ser	Leu	Asp	Gly	Lys	Lys	Trp	Gln	Thr	Tyr	Arg	Gly	Asn	Ser	Thr	Gly	
2110					2115					2120						
acc	tta	atg	gtc	ttc	ttt	ggc	aat	gtg	gat	tca	tct	ggg	ata	aaa	cac	6618
Thr	Leu	Met	Val	Phe	Phe	Gly	Asn	Val	Asp	Ser	Ser	Gly	Ile	Lys	His	
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Asn	Ile	Phe	Asn	Pro	Pro	Ile	Ile	Ala	Arg	Tyr	Ile	Arg	Leu	His	Pro	
2140					2145					2150						

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Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys	
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gat tta aat agt tgc agc atg cca ttg gga atg gag agt aaa gca ata	6762
Asp Leu Asn Ser Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile	
2170 2175 2180 2185	
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Ser Asp Ala Gln Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala	
2190 2195 2200	
acc tgg tct cct tca aaa gct cga ctt cac ctc caa ggg agg agt aat	6858
Thr Trp Ser Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn	
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Ala Trp Arg Pro Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp	
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Phe Gln Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys	
2235 2240 2245	
tct ctg ctt acc agc atg tat gtg aag gag ttc ctc atc tcc agc agt	7002
Ser Leu Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser	
2250 2255 2260 2265	
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Gln Asp Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys	
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Val Phe Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu	
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Asp Leu Tyr	
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<212> PRT
<213> Homo sapiens

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Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro
 20          25          30
Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys
 35          40          45
Thr Leu Phe Val Glu Phe Thr Val His Leu Phe Asn Ile Ala Lys Pro
 50          55          60
Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val
 65          70          75          80
Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val
 85          90          95
Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Glu Ala
 100          105          110
Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
 115          120          125
Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
 130          135          140
Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser
 145          150          155          160
His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu
 165          170          175
Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu
 180          185          190
His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
 195          200          205
His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser
 210          215          220
Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg
 225          230          235          240
Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His
 245          250          255
Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu
 260          265          270
Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile
 275          280          285
Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly
 290          295          300
Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met
 305          310          315          320
Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg
 325          330          335
Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp
 340          345          350
Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe
 355          360          365
Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His

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370		375		380
Tyr Ile Ala Ala Glu	Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu			
385	390	395	400	
Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro				
405	410	415		
Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr				
420	425	430		
Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile				
435	440	445		
Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile				
450	455	460		
Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile				
465	470	475	480	
Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys Gly Val Lys				
485	490	495		
His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys				
500	505	510		
Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys				
515	520	525		
Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala				
530	535	540		
Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp				
545	550	555	560	
Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe				
565	570	575		
Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln				
580	585	590		
Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe				
595	600	605		
Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser				
610	615	620		
Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu				
625	630	635	640	
Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr				
645	650	655		
Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro				
660	665	670		
Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp				
675	680	685		
Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala				
690	695	700		
Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu				
705	710	715	720	
Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala				
725	730	735		
Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Pro Ser Thr Arg				
740	745	750		
Gln Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp Ile Glu Lys				
755	760	765		
Thr Asp Pro Trp Phe Ala His Arg Thr Pro Met Pro Lys Ile Gln Asn				
770	775	780		
Val Ser Ser Ser Asp Leu Leu Met Leu Leu Arg Gln Ser Pro Thr Pro				
785	790	795	800	
His Gly Leu Ser Leu Ser Asp Leu Gln Glu Ala Lys Tyr Glu Thr Phe				
805	810	815		
Ser Asp Asp Pro Ser Pro Gly Ala Ile Asp Ser Asn Asn Ser Leu Ser				
820	825	830		
Glu Met Thr His Phe Arg Pro Gln Leu His His Ser Gly Asp Met Val				
835	840	845		
Phe Thr Pro Glu Ser Gly Leu Gln Leu Arg Leu Asn Glu Lys Leu Gly				
850	855	860		
Thr Thr Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys Val Ser Ser				
865	870	875	880	
Thr Ser Asn Asn Leu Ile Ser Thr Ile Pro Ser Asp Asn Leu Ala Ala				
885	890	895		
Gly Thr Asp Asn Thr Ser Ser Leu Gly Pro Pro Ser Met Pro Val His				



1425		1430		1435		1440
Asn Asn Leu Ser	Leu Ala Ile Leu Thr	Leu Glu Met Thr Gly	Asp Gln			
	1445	1450	1455			
Arg Glu Val Gly	Ser Leu Gly Thr Ser	Ala Thr Asn Ser	Val Thr Tyr			
	1460	1465	1470			
Lys Lys Val Glu	Asn Thr Val Leu Pro	Lys Pro Asp Leu	Pro Lys Thr			
	1475	1480	1485			
Ser Gly Lys Val	Glu Leu Leu Pro	Lys Val His Ile	Tyr Gln Lys Asp			
	1490	1495	1500			
Leu Phe Pro Thr	Glu Thr Ser Asn	Gly Ser Pro Gly	His Leu Asp Leu			
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Val Glu Gly Ser	Leu Leu Gln Gly	Thr Glu Gly Ala	Ile Lys Trp Asn			
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Glu Ala Asn Arg	Pro Gly Lys Val	Pro Phe Leu Arg	Val Ala Thr Glu			
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Lys Ser Pro Glu	Lys Thr Ala Phe	Lys Lys Lys Asp	Thr Ile Leu Ser			
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Glu Arg Leu Cys	Ser Gln Asn Pro	Val Leu Lys Arg	His Gln Arg			
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Glu Ile Thr Arg	Thr Thr Leu Gln	Ser Asp Gln Glu	Glu Ile Asp Tyr			
	1650	1655	1660			
Asp Asp Thr Ile	Ser Val Glu Met	Lys Lys Glu Asp	Phe Asp Ile Tyr			
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Asp Glu Asp Glu	Asn Gln Ser Pro	Arg Ser Phe Gln	Lys Lys Thr Arg			
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His Tyr Phe Ile	Ala Ala Val Glu	Arg Leu Trp Asp	Tyr Gly Met Ser			
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Ser Ser Pro His	Val Leu Arg Asn	Arg Ala Gln Ser	Gly Ser Val Pro			
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Gln Phe Lys Lys	Val Val Phe Gln	Glu Phe Thr Asp	Gly Ser Phe Thr			
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Gln Pro Leu Tyr	Arg Gly Glu Leu	Asn Glu His Leu	Gly Leu Leu Gly			
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Pro Tyr Ile Arg	Ala Glu Val Glu	Asp Asn Ile Met	Val Thr Phe Arg			
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Glu Glu Asp Gln	Arg Gln Gly Ala	Glu Pro Arg Lys	Asn Phe Val Lys			
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Pro Asn Glu Thr	Lys Thr Tyr Phe	Trp Lys Val Gln	His His Met Ala			
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Pro Thr Lys Asp	Glu Phe Asp Cys	Lys Ala Trp Ala	Tyr Phe Ser Asp			
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Val Asp Leu Glu	Lys Asp Val His	Ser Gly Leu Ile	Gly Pro Leu Leu			
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Val Cys His Thr	Asn Thr Leu Asn	Pro Ala His Gly	Arg Gln Val Thr			
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Val Gln Glu Phe	Ala Leu Phe Phe	Thr Ile Phe Asp	Glu Thr Lys Ser			
	1875	1880	1885			
Trp Tyr Phe Thr	Glu Asn Met Glu	Arg Asn Cys Arg	Ala Pro Cys Asn			
	1890	1895	1900			
Ile Gln Met Glu	Asp Pro Thr Phe	Lys Glu Asn Tyr	Arg Phe His Ala			
	1905	1910	1915			1920
Ile Asn Gly Tyr	Ile Met Asp Thr	Leu Pro Gly Leu	Val Met Ala Gln			
	1925	1930	1935			
Asp Gln Arg Ile	Arg Trp Tyr Leu	Leu Ser Met Gly	Ser Asn Glu Asn			
	1940	1945	1950			
Ile His Ser Ile	His Phe Ser Gly	His Val Phe Thr	Val Arg Lys Lys			

1955					1960					1965						
Glu	Glu	Tyr	Lys	Met	Ala	Leu	Tyr	Asn	Leu	Tyr	Pro	Gly	Val	Phe	Glu	
1970					1975					1980						
Thr	Val	Glu	Met	Leu	Pro	Ser	Lys	Ala	Gly	Ile	Trp	Arg	Val	Glu	Cys	
1985					1990					1995					2000	
Leu	Ile	Gly	Glu	His	Leu	His	Ala	Gly	Met	Ser	Thr	Leu	Phe	Leu	Val	
2005					2010					2015						
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Tyr	Asn	His	Ser	Thr	Thr	Asn	Glu	Lys	Leu	His	Thr	Glu	Ser	Pro	Thr
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Ser	Ile	Glu	Asn	Ser	Thr	Thr	Asp	Leu	Gln	Asp	Ala	Ile	Leu	Lys	Val
				1045					1050					1055	
Asn	Ser	Glu	Ile	Gln	Glu	Val	Thr	Ala	Leu	Ile	His	Asp	Gly	Thr	Leu
				1060				1065						1070	
Leu	Gly	Lys	Asn	Ser	Thr	Tyr	Leu	Arg	Leu	Asn	His	Met	Leu	Asn	Arg
		1075						1080					1085		
Thr	Thr	Ser	Thr	Lys	Asn	Lys	Asp	Ile	Phe	His	Arg	Lys	Asp	Glu	Asp
				1090			1095					1100			
Pro	Ile	Pro	Gln	Asp	Glu	Glu	Asn	Thr	Ile	Met	Pro	Phe	Ser	Lys	Met
1105					1110					1115					1120
Leu	Phe	Leu	Ser	Glu	Ser	Ser	Asn	Trp	Phe	Lys	Lys	Thr	Asn	Gly	Asn
				1125					1130					1135	
Asn	Ser	Leu	Asn	Ser	Glu	Gln	Glu	His	Ser	Pro	Lys	Gln	Leu	Val	Tyr
			1140					1145					1150		



Leu Met Phe Lys Lys Tyr Val Lys Asn Gln Ser Phe Leu Ser Glu Lys  
 1155 1160 1165  
 Asn Lys Val Thr Val Glu Gln Asp Gly Phe Thr Lys Asn Ile Gly Leu  
 1170 1175 1180  
 Lys Asp Met Ala Phe Pro His Asn Met Ser Ile Phe Leu Thr Thr Leu  
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 Ser Asn Val His Glu Asn Gly Arg His Asn Gln Glu Lys Asn Ile Gln  
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 Glu Glu Ile Glu Lys Glu Ala Leu Ile Glu Glu Lys Val Val Leu Pro  
 1220 1225 1230  
 Gln Val His Glu Ala Thr Gly Ser Lys Asn Phe Leu Lys Asp Ile Leu  
 1235 1240 1245  
 Ile Leu Gly Thr Arg Gln Asn Ile Ser Leu Tyr Glu Val His Val Pro  
 1250 1255 1260  
 Val Leu Gln Asn Ile Thr Ser Ile Asn Asn Ser Thr Asn Thr Val Gln  
 1265 1270 1275 1280  
 Ile His Met Glu His Phe Phe Lys Arg Arg Lys Asp Lys Glu Thr Asn  
 1285 1290 1295  
 Ser Glu Gly Leu Val Asn Lys Thr Arg Glu Met Val Lys Asn Tyr Pro  
 1300 1305 1310  
 Ser Gln Lys Asn Ile Thr Thr Gln Arg Ser Lys Arg Ala Leu Gly Gln  
 1315 1320 1325  
 Phe Arg Leu Ser Thr Gln Trp Leu Lys Thr Ile Asn Cys Ser Thr Gln  
 1330 1335 1340  
 Cys Ile Ile Lys Gln Ile Asp His Ser Lys Glu Met Lys Lys Phe Ile  
 1345 1350 1355 1360  
 Thr Lys Ser Ser Leu Ser Asp Ser Ser Val Ile Lys Ser Thr Thr Gln  
 1365 1370 1375  
 Thr Asn Ser Ser Asp Ser His Ile Val Lys Thr Ser Ala Phe Pro Pro  
 1380 1385 1390  
 Ile Asp Leu Lys Arg Ser Pro Phe Gln Asn Lys Phe Ser His Val Gln  
 1395 1400 1405  
 Ala Ser Ser Tyr Ile Tyr Asp Phe Lys Thr Lys Ser Ser Arg Ile Gln  
 1410 1415 1420  
 Glu Ser Asn Asn Phe Leu Lys Glu Thr Lys Ile Asn Asn Pro Ser Leu  
 1425 1430 1435 1440  
 Ala Ile Leu Pro Trp Asn Met Phe Ile Asp Gln Gly Lys Phe Thr Ser  
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 Pro Gly Lys Ser Asn Thr Asn Ser Val Thr Tyr Lys Lys Arg Glu Asn  
 1460 1465 1470  
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 Gly Glu Ser Ile Lys Gly Lys Thr Glu Ser Ser Lys Asn Thr Arg Ser  
 1540 1545 1550  
 Lys Leu Leu Asn His His Ala Trp Asp Tyr His Tyr Ala Ala Gln Ile  
 1555 1560 1565  
 Pro Lys Asp Met Trp Lys Ser Lys Glu Lys Ser Pro Glu Ile Ile Ser  
 1570 1575 1580  
 Ile Lys Gln Glu Asp Thr Ile Leu Ser Leu Arg Pro His Gly Asn Ser  
 1585 1590 1595 1600  
 His Ser Ile Gly Ala Asn Glu Lys Gln Asn Trp Pro Gln Arg Glu Thr  
 1605 1610 1615  
 Thr Trp Val Lys Gln Gly Gln Thr Gln Arg Thr Cys Ser Gln Ile Pro  
 1620 1625 1630  
 Pro Val Leu Lys Arg His Gln Arg Glu Leu Ser Ala Phe Gln Ser Glu  
 1635 1640 1645  
 Gln Glu Ala Thr Asp Tyr Asp Asp Ala Ile Thr Ile Glu Thr Ile Glu  
 1650 1655 1660  
 Asp Phe Asp Ile Tyr Ser Glu Asp Ile Lys Gln Gly Pro Arg Ser Phe  
 1665 1670 1675 1680

Gln	Gln	Lys	Thr	Arg	His	Tyr	Phe	Ile	Ala	Ala	Val	Glu	Arg	Leu	Trp	1685	1690	1695
Asp	Tyr	Gly	Met	Ser	Thr	Ser	His	Val	Leu	Arg	Asn	Arg	Tyr	Gln	Ser	1700	1705	1710
Asp	Asn	Val	Pro	Gln	Phe	Lys	Lys	Val	Val	Phe	Gln	Glu	Phe	Thr	Asp	1715	1720	1725
Gly	Ser	Phe	Ser	Gln	Pro	Leu	Tyr	Arg	Gly	Glu	Leu	Asn	Glu	His	Leu	1730	1735	1740
Gly	Leu	Leu	Gly	Pro	Tyr	Ile	Arg	Ala	Glu	Val	Glu	Asp	Asn	Ile	Met	1745	1750	1755
Val	Thr	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser	Ser	1765	1770	1775
Leu	Ile	Ser	Tyr	Lys	Glu	Asp	Gln	Arg	Gly	Glu	Glu	Pro	Arg	Arg	Asn	1780	1785	1790
Phe	Val	Lys	Pro	Asn	Glu	Thr	Lys	Ile	Tyr	Phe	Trp	Lys	Val	Gln	His	1795	1800	1805
His	Met	Ala	Pro	Thr	Glu	Asp	Glu	Phe	Asp	Cys	Lys	Ala	Trp	Ala	Tyr	1810	1815	1820
Phe	Ser	Asp	Val	Asp	Leu	Glu	Arg	Asp	Met	His	Ser	Gly	Leu	Ile	Gly	1825	1830	1835
Pro	Leu	Leu	Ile	Cys	His	Ala	Asn	Thr	Leu	Asn	Pro	Ala	His	Gly	Arg	1845	1850	1855
Gln	Val	Ser	Val	Gln	Glu	Phe	Ala	Leu	Leu	Phe	Thr	Ile	Phe	Asp	Glu	1860	1865	1870
Thr	Lys	Ser	Trp	Tyr	Phe	Thr	Glu	Asn	Val	Lys	Arg	Asn	Cys	Lys	Thr	1875	1880	1885
Pro	Cys	Asn	Phe	Gln	Met	Glu	Asp	Pro	Thr	Leu	Lys	Glu	Asn	Tyr	Arg	1890	1895	1900
Phe	His	Ala	Ile	Asn	Gly	Tyr	Val	Met	Asp	Thr	Leu	Pro	Gly	Leu	Val	1905	1910	1915
Met	Ala	Gln	Asp	Gln	Arg	Ile	Arg	Trp	Tyr	Leu	Leu	Ser	Met	Gly	Asn	1925	1930	1935
Asn	Glu	Asn	Ile	Gln	Ser	Ile	His	Phe	Ser	Gly	His	Val	Phe	Thr	Val	1940	1945	1950
Arg	Lys	Lys	Glu	Glu	Tyr	Lys	Met	Ala	Val	Tyr	Asn	Leu	Tyr	Pro	Gly	1955	1960	1965
Val	Phe	Glu	Thr	Leu	Glu	Met	Ile	Pro	Ser	Arg	Ala	Gly	Ile	Trp	Arg	1970	1975	1980
Val	Glu	Cys	Leu	Ile	Gly	Glu	His	Leu	Gln	Ala	Gly	Met	Ser	Thr	Leu	1985	1990	1995
Phe	Leu	Val	Tyr	Ser	Lys	Gln	Cys	Gln	Ile	Pro	Leu	Gly	Met	Ala	Ser	2005	2010	2015
Gly	Ser	Ile	Arg	Asp	Phe	Gln	Ile	Thr	Ala	Ser	Gly	His	Tyr	Gly	Gln	2020	2025	2030
Trp	Ala	Pro	Asn	Leu	Ala	Arg	Leu	His	Tyr	Ser	Gly	Ser	Ile	Asn	Ala	2035	2040	2045
Trp	Ser	Thr	Lys	Glu	Pro	Phe	Ser	Trp	Ile	Lys	Val	Asp	Leu	Leu	Ala	2050	2055	2060
Pro	Met	Ile	Val	His	Gly	Ile	Lys	Thr	Gln	Gly	Ala	Arg	Gln	Lys	Phe	2065	2070	2075
Ser	Ser	Leu	Tyr	Ile	Ser	Gln	Phe	Ile	Ile	Met	Tyr	Ser	Leu	Asp	Gly	2085	2090	2095
Lys	Lys	Trp	Leu	Ser	Tyr	Gln	Gly	Asn	Ser	Thr	Gly	Thr	Leu	Met	Val	2100	2105	2110
Phe	Phe	Gly	Asn	Val	Asp	Ser	Ser	Gly	Ile	Lys	His	Asn	Ser	Phe	Asn	2115	2120	2125
Pro	Pro	Ile	Ile	Ala	Arg	Tyr	Ile	Arg	Leu	His	Pro	Thr	His	Ser	Ser	2130	2135	2140
Ile	Arg	Ser	Thr	Leu	Arg	Met	Glu	Leu	Met	Gly	Cys	Asp	Leu	Asn	Ser	2145	2150	2155
Cys	Ser	Ile	Pro	Leu	Gly	Met	Glu	Ser	Lys	Val	Ile	Ser	Asp	Thr	Gln	2165	2170	2175
Ile	Thr	Ala	Ser	Ser	Tyr	Phe	Thr	Asn	Met	Phe	Ala	Thr	Trp	Ser	Pro	2180	2185	2190
Ser	Gln	Ala	Arg	Leu	His	Leu	Gln	Gly	Arg	Thr	Asn	Ala	Trp	Arg	Pro	2195	2200	2205

Gln Val Asn Asp Pro Lys Gln Trp Leu Gln Val Asp Leu Gln Lys Thr  
 2210 2215 2220  
 Met Lys Val Thr Gly Ile Ile Thr Gln Gly Val Lys Ser Leu Phe Thr  
 2225 2230 2235 2240  
 Ser Met Phe Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His  
 2245 2250 2255  
 His Trp Thr Gln Ile Leu Tyr Asn Gly Lys Val Lys Val Phe Gln Gly  
 2260 2265 2270  
 Asn Gln Asp Ser Ser Thr Pro Met Met Asn Ser Leu Asp Pro Pro Leu  
 2275 2280 2285  
 Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ile Trp Glu His Gln Ile  
 2290 2295 2300  
 Ala Leu Arg Leu Glu Ile Leu Gly Cys Glu Ala Gln Gln Gln Tyr  
 2305 2310 2315

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<400> 10  
 Arg His Gln Arg  
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(HSQ)

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Met	Gln	Ile	Glu	Leu	Ser	Thr	Cys	Phe	Phe	Leu	Cys	Leu	Leu	Arg	Phe	
1				5					10					15		
tgc	ttt	agt	gcc	acc	aga	aga	tac	tac	ctg	ggc	gca	gtg	gaa	ctg	tca	96
Cys	Phe	Ser	Ala	Thr	Arg	Arg	Tyr	Tyr	Leu	Gly	Ala	Val	Glu	Leu	Ser	
			20					25					30			
tgg	gac	tat	atg	caa	agt	gat	ctc	ggc	gag	ctg	cct	gtg	gac	gca	aga	144
Trp	Asp	Tyr	Met	Gln	Ser	Asp	Leu	Gly	Glu	Leu	Pro	Val	Asp	Ala	Arg	
		35					40					45				
ttt	cct	cct	aga	gtg	cca	aaa	tct	ttt	cca	ttc	aac	acc	tca	gtc	gtg	192
Phe	Pro	Pro	Arg	Val	Pro	Lys	Ser	Phe	Pro	Phe	Asn	Thr	Ser	Val	Val	
	50					55					60					
tac	aaa	aag	act	ctg	ttt	gta	gaa	ttc	acg	ggt	cac	ctt	ttc	aac	atc	240
Tyr	Lys	Lys	Thr	Leu	Phe	Val	Glu	Phe	Thr	Val	His	Leu	Phe	Asn	Ile	
	65				70				75						80	
gct	aag	cca	agg	cca	ccc	tgg	atg	ggc	ctg	cta	ggc	cct	acc	atc	cag	288
Ala	Lys	Pro	Arg	Pro	Pro	Trp	Met	Gly	Leu	Leu	Gly	Pro	Thr	Ile	Gln	
				85					90					95		
gct	gag	ggt	tat	gat	aca	gtg	gtc	att	aca	ctt	aag	aac	atg	gct	tcc	336
Ala	Glu	Val	Tyr	Asp	Thr	Val	Val	Ile	Thr	Leu	Lys	Asn	Met	Ala	Ser	
			100					105					110			
cat	cct	gtc	agt	ctt	cat	gct	ggt	gta	tcc	tac	tgg	aaa	gct	tct		384
His	Pro	Val	Ser	Leu	His	Ala	Val	Gly	Val	Ser	Tyr	Trp	Lys	Ala	Ser	
		115					120				125					
gag	gga	gct	gaa	tat	gat	gat	cag	acc	agt	caa	agg	gag	aaa	gaa	gat	432
Glu	Gly	Ala	Glu	Tyr	Asp	Asp	Gln	Thr	Ser	Gln	Arg	Glu	Lys	Glu	Asp	
	130					135					140					
gat	aaa	gtc	ttc	cct	ggc	gga	agc	cat	aca	tat	gtc	tgg	cag	gtc	ctg	480
Asp	Lys	Val	Phe	Pro	Gly	Gly	Ser	His	Thr	Tyr	Val	Trp	Gln	Val	Leu	
	145				150					155					160	
aaa	gag	aat	ggc	cca	atg	gcc	tct	gac	cca	ctg	tgc	ctt	acc	tac	tca	528
Lys	Glu	Asn	Gly	Pro	Met	Ala	Ser	Asp	Pro	Leu	Cys	Leu	Thr	Tyr	Ser	
			165					170						175		
tat	ctt	tct	cat	gtg	gac	ctg	gta	aaa	gac	ttg	aat	tca	ggc	ctc	att	576
Tyr	Leu	Ser	His	Val	Asp	Leu	Val	Lys	Asp	Leu	Asn	Ser	Gly	Leu	Ile	
			180					185					190			
gga	gcc	cta	cta	gta	tgt	aga	gaa	ggg	agt	ctg	gcc	aag	gaa	aag	aca	624
Gly	Ala	Leu	Leu	Val	Cys	Arg	Glu	Gly	Ser	Leu	Ala	Lys	Glu	Lys	Thr	
		195					200					205				
cag	acc	ttg	cac	aaa	ttt	ata	cta	ctt	ttt	gct	gta	ttt	gat	gaa	ggg	672
Gln	Thr	Leu	His	Lys	Phe	Ile	Leu	Leu	Phe	Ala	Val	Phe	Asp	Glu	Gly	
	210					215					220					
aaa	agt	tgg	cac	tca	gaa	aca	aag	aac	tcc	ttg	atg	cag	gat	agg	gat	720
Lys	Ser	Trp	His	Ser		Thr	Lys	Asn	Ser		Met	Gln	Asp	Arg	Asp	
	225				230					235					240	
gct	gca	tct	gct	cgg	gcc	tgg	cct	aaa	atg	cac	aca	gtc	aat	ggc	tat	768

Ala	Ala	Ser	Ala	Arg	Ala	Trp	Pro	Lys	Met	His	Thr	Val	Asn	Gly	Tyr		
				245					250					255			
gta	aac	agg	tct	ctg	cca	ggg	ctg	att	gga	tgc	cac	agg	aaa	tca	gtc	816	
Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Arg	Lys	Ser	Val		
			260					265					270				
tat	tgg	cat	gtg	att	gga	atg	ggc	acc	act	cct	gaa	gtg	cac	tca	ata	864	
Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Thr	Pro	Glu	Val	His	Ser	Ile		
		275					280					285					
ttc	ctc	gaa	ggg	cac	aca	ttt	ctt	gtg	agg	aac	cat	cgc	cag	gcg	tcc	912	
Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	Asn	His	Arg	Gln	Ala	Ser		
	290					295					300						
ttg	gaa	atc	tcg	cca	ata	act	ttc	ctt	act	gct	caa	aca	ctc	ttg	atg	960	
Leu	Glu	Ile	Ser	Pro	Ile	Thr	Phe	Leu	Thr	Ala	Gln	Thr	Leu	Leu	Met		
305					310					315					320		
gac	ctt	gga	cag	ttt	cta	ctg	ttt	tgt	cat	atc	tct	tcc	cac	caa	cat	1008	
Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	Gln	His		
			325					330						335			
gat	ggc	atg	gaa	gct	tat	gtc	aaa	gta	gac	agc	tgt	cca	gag	gaa	ccc	1056	
Asp	Gly	Met	Glu	Ala	Tyr	Val	Lys	Val	Asp	Ser	Cys	Pro	Glu	Glu	Pro		
			340					345					350				
caa	cta	cga	atg	aaa	aat	aat	gaa	gaa	gcg	gaa	gac	tat	gat	gat	gat	1104	
Gln	Leu	Arg	Met	Lys	Asn	Asn	Glu	Glu	Ala	Glu	Asp	Tyr	Asp	Asp	Asp		
		355					360					365					
ctt	act	gat	tct	gaa	atg	gat	gtg	gtc	agg	ttt	gat	gat	gac	aac	tct	1152	
Leu	Thr	Asp	Ser	Glu	Met	Asp	Val	Val	Arg	Phe	Asp	Asp	Asp	Asn	Ser		
	370					375					380						
cct	tcc	ttt	atc	caa	att	cgc	tca	gtt	gcc	aag	aag	cat	cct	aaa	act	1200	
Pro	Ser	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr		
385					390					395					400		
tgg	gta	cat	tac	att	gct	gct	gaa	gag	gag	gac	tgg	gac	tat	gct	ccc	1248	
Trp	Val	His	Tyr	Ile	Ala	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro		
			405					410						415			
tta	gtc	ctc	gcc	ccc	gat	gac	aga	agt	tat	aaa	agt	caa	tat	ttg	aac	1296	
Leu	Val	Leu	Ala	Pro	Asp	Asp	Arg	Ser	Tyr	Lys	Ser	Gln	Tyr	Leu	Asn		
			420					425					430				
aat	ggc	cct	cag	cgg	att	ggg	agg	aag	tac	aaa	aaa	gtc	cga	ttt	atg	1344	
Asn	Gly	Pro	Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Val	Arg	Phe	Met		
		435					440					445					
gca	tac	aca	gat	gaa	acc	ttt	aag	acg	cgt	gaa	gct	att	cag	cat	gaa	1392	
Ala	Tyr	Thr	Asp	Glu	Thr	Phe	Lys	Thr	Arg	Glu	Ala	Ile	Gln	His	Glu		
	450					455					460						
tca	gga	atc	ttg	gga	cct	tta	ctt	tat	ggg	gaa	gtt	gga	gac	aca	ctg	1440	
Ser	Gly	Ile	Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	Val	Gly	Asp	Thr	Leu		
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ttg	att	ata	ttt	aag	aat	caa	gca	agc	aga	cca	tat	aac	atc	tac	cct	1488	
Leu	Ile	Ile	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro		
			485						490					495			
cac	gga	atc	act	gat	gtc	cgt	cct	ttg	tat	tca	agg	aga	tta	cca	aaa	1536	
His	Gly	Ile	Thr	Asp	Val	Arg	Pro	Leu	Tyr	Ser	Arg	Arg	Leu	Pro	Lys		
			500					505						510			

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Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe	
515 520 525	
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Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp	
530 535 540	
ccg cgg tgc ctg acc cgc tat tac tct agt ttc gtt aat atg gag aga	1680
Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg	
545 550 555 560	
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Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu	
565 570 575	
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Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val	
580 585 590	
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Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu	
595 600 605	
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Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp	
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cca gag ttc caa gcc tcc aac atc atg cac agc atc aat ggc tat gtt	1920
Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val	
625 630 635 640	
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Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp	
645 650 655	
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Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe	
660 665 670	
tct gga tat acc ttc aaa cac aaa atg gtc tat gaa gac aca ctc acc	2064
Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr	
675 680 685	
cta ttc cca ttc tca gga gaa act gtc ttc atg tcg atg gaa aac cca	2112
Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro	
690 695 700	
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Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly	
705 710 715 720	
atg acc gcc tta ctg aag gtt tct agt tgt gac aag aac act ggt gat	2208
Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp	
725 730 735	
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Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys	
740 745 750	
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Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Pro Pro Val Leu	
755 760 765	
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Lys	Arg	His	Gln	Arg	Glu	Ile	Thr	Arg	Thr	Thr	Leu	Gln	Ser	Asp	Gln		
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Glu	Glu	Ile	Asp	Tyr	Asp	Asp	Thr	Ile	Ser	Val	Glu	Met	Lys	Lys	Glu		
785					790				795						800		
gat	ttt	gac	att	tat	gat	gag	gat	gaa	aat	cag	agc	ccc	cgc	agc	ttt	2448	
Asp	Phe	Asp	Ile	Tyr	Asp	Glu	Asp	Glu	Asn	Gln	Ser	Pro	Arg	Ser	Phe		
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Gln	Lys	Lys	Thr	Arg	His	Tyr	Phe	Ile	Ala	Ala	Val	Glu	Arg	Leu	Trp		
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Asp	Tyr	Gly	Met	Ser	Ser	Ser	Pro	His	Val	Leu	Arg	Asn	Arg	Ala	Gln		
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agt	ggc	agt	gtc	cct	cag	ttc	aag	aaa	gtt	gtt	ttc	cag	gaa	ttt	act	2592	
Ser	Gly	Ser	Val	Pro	Gln	Phe	Lys	Lys	Val	Val	Phe	Gln	Glu	Phe	Thr		
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Asp	Gly	Ser	Phe	Thr	Gln	Pro	Leu	Tyr	Arg	Gly	Glu	Leu	Asn	Glu	His		
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Met	Val	Thr	Phe	Arg	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser		
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Ser	Leu	Ile	Ser	Tyr	Glu	Glu	Asp	Gln	Arg	Gln	Gly	Ala	Glu	Pro	Arg		
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Lys	Asn	Phe	Val	Lys	Pro	Asn	Glu	Thr	Lys	Thr	Tyr	Phe	Trp	Lys	Val		
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Ala	Tyr	Phe	Ser	Asp	Val	Asp	Leu	Glu	Lys	Asp	Val	His	Ser	Gly	Leu		
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Ile	Gly	Pro	Leu	Leu	Val	Cys	His	Thr	Asn	Thr	Leu	Asn	Pro	Ala	His		
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Gly	Arg	Gln	Val	Thr	Val	Gln	Glu	Phe	Ala	Leu	Phe	Phe	Thr	Ile	Phe		
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Asp	Glu	Thr	Lys	Ser	Trp	Tyr	Phe	Thr	Glu	Asn	Met	Glu	Arg	Asn	Cys		
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Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly	
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Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe	
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Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr	
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Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile	
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Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu	
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Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu	
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Ser	Pro	Ser	Lys	Ala	Arg	Leu	His	Leu	Gln	Gly	Arg	Ser	Asn	Ala	Trp	
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Gln	Gly	Asn	Gln	Asp	Ser	Phe	Thr	Pro	Val	Val	Asn	Ser	Leu	Asp	Pro	
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Pro	Leu	Leu	Thr	Arg	Tyr	Leu	Arg	Ile	His	Pro	Gln	Ser	Trp	Val	His	
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tac																4371
Tyr																

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Trp	Asp	Tyr	Met	Gln	Ser	Asp	Leu	Gly	Glu	Leu	Pro	Val	Asp	Ala	Arg
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Phe	Pro	Pro	Arg	Val	Pro	Lys	Ser	Phe	Pro	Phe	Asn	Thr	Ser	Val	Val
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Tyr	Lys	Lys	Thr	Leu	Phe	Val	Glu	Phe	Thr	Val	His	Leu	Phe	Asn	Ile
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Ala	Lys	Pro	Arg	Pro	Pro	Trp	Met	Gly	Leu	Leu	Gly	Pro	Thr	Ile	Gln
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Ala	Glu	Val	Tyr	Asp	Thr	Val	Val	Ile	Thr	Leu	Lys	Asn	Met	Ala	Ser
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His	Pro	Val	Ser	Leu	His	Ala	Val	Gly	Val	Ser	Tyr	Trp	Lys	Ala	Ser
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Glu	Gly	Ala	Glu	Tyr	Asp	Asp	Gln	Thr	Ser	Gln	Arg	Glu	Lys	Glu	Asp
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Asp	Lys	Val	Phe	Pro	Gly	Gly	Ser	His	Thr	Tyr	Val	Trp	Gln	Val	Leu
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Lys	Glu	Asn	Gly	Pro	Met	Ala	Ser	Asp	Pro	Leu	Cys	Leu	Thr	Tyr	Ser
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Tyr	Leu	Ser	His	Val	Asp	Leu	Val	Lys	Asp	Leu	Asn	Ser	Gly	Leu	Ile
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Gly	Ala	Leu	Leu	Val	Cys	Arg	Glu	Gly	Ser	Leu	Ala	Lys	Glu	Lys	Thr
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Gln	Thr	Leu	His	Lys	Phe	Ile	Leu	Leu	Phe	Ala	Val	Phe	Asp	Glu	Gly
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Lys	Ser	Trp	His	Ser	Glu	Thr	Lys	Asn	Ser	Leu	Met	Gln	Asp	Arg	Asp
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Ala	Ala	Ser	Ala	Arg	Ala	Trp	Pro	Lys	Met	His	Thr	Val	Asn	Gly	Tyr
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Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Arg	Lys	Ser	Val
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Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Thr	Pro	Glu	Val	His	Ser	Ile
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Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	Asn	His	Arg	Gln	Ala	Ser
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Leu	Glu	Ile	Ser	Pro	Ile	Thr	Phe	Leu	Thr	Ala	Gln	Thr	Leu	Leu	Met
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Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	Gln	His
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Asp	Gly	Met	Glu	Ala	Tyr	Val	Lys	Val	Asp	Ser	Cys	Pro	Glu	Glu	Pro
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Gln	Leu	Arg	Met	Lys	Asn	Asn	Glu	Glu	Ala	Glu	Asp	Tyr	Asp	Asp	Asp
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Leu	Thr	Asp	Ser	Glu	Met	Asp	Val	Val	Arg	Phe	Asp	Asp	Asp	Asn	Ser
	370					375					380				
Pro	Ser	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr
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Trp	Val	His	Tyr	Ile	Ala	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro
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Leu	Val	Leu	Ala	Pro	Asp	Asp	Arg	Ser	Tyr	Lys	Ser	Gln	Tyr	Leu	Asn
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Ala	Tyr	Thr	Asp	Glu	Thr	Phe	Lys	Thr	Arg	Glu	Ala	Ile	Gln	His	Glu
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Leu	Ile	Ile	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro
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His	Gly	Ile	Thr	Asp	Val	Arg	Pro	Leu	Tyr	Ser	Arg	Arg	Leu	Pro	Lys
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Gly	Val	Lys	His	Leu	Lys	Asp	Phe	Pro	Ile	Leu	Pro	Gly	Glu	Ile	Phe
		515					520					525			
Lys	Tyr	Lys	Trp	Thr	Val	Thr	Val	Glu	Asp	Gly	Pro	Thr	Lys	Ser	Asp
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Pro	Arg	Cys	Leu	Thr	Arg	Tyr	Tyr	Ser	Ser	Phe	Val	Asn	Met	Glu	Arg
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Asp	Leu	Ala	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Tyr	Lys	Glu
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Ser	Val	Asp	Gln	Arg	Gly	Asn	Gln	Ile	Met	Ser	Asp	Lys	Arg	Asn	Val
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Pro	Glu	Phe	Gln	Ala	Ser	Asn	Ile	Met	His	Ser	Ile	Asn	Gly	Tyr	Val
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Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp
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Tyr	Tyr	Glu	Asp	Ser	Tyr	Glu	Asp	Ile	Ser	Ala	Tyr	Leu	Leu	Ser	Lys
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 Ser Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp  
 1330 1335 1340  
 Arg Pro Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln  
 1345 1350 1355 1360  
 Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu  
 1365 1370 1375  
 Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp  
 1380 1385 1390  
 Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe  
 1395 1400 1405  
 Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro  
 1410 1415 1420  
 Pro Leu Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His  
 1425 1430 1435 1440  
 Gln Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu  
 1445 1450 1455  
 Tyr

<210> 14  
 <211> 4401  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> hybrid human and porcine factor VIII sequence

<221> CDS  
 <222> (1)...(4401)  
 <223> HP44/OL-- factor VIII having the following  
 domains: Alp-A2p-app-A3p-C1h-C2h

<400> 14  
 atg cag cta gag ctc tcc acc tgt gtc ttt ctg tgt ctc ttg cca ctc 48  
 Met Gln Leu Glu Leu Ser Thr Cys Val Phe Leu Cys Leu Leu Pro Leu  
 1 5 10 15  
 ggc ttt agt gcc atc agg aga tac tac ctg ggc gca gtg gaa ctg tcc 96  
 Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser  
 20 25 30  
 tgg gac tac cgg caa agt gaa ctc ctc cgt gag ctg cac gtg gac acc 144  
 Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr  
 35 40 45  
 aga ttt cct gct aca gcg cca gga gct ctt ccg ttg ggc ccg tca gtc 192  
 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val

50	55	60	
ctg tac aaa aag act	gtg ttc gta gag ttc	acg gat caa ctt ttc agc	240
Leu Tyr Lys Lys Thr	Val Phe Val Glu Phe Thr	Asp Gln Leu Phe Ser	
65	70	75 80	
ggt gcc agg ccc agg	cca cca tgg atg ggt	ctg ctg ggt cct acc atc	288
Val Ala Arg Pro Arg	Pro Pro Trp Met Gly	Leu Leu Gly Pro Thr Ile	
	85	90 95	
cag gct gag gtt tac	gac acg gtg gtc gtt	acc ctg aag aac atg gct	336
Gln Ala Glu Val Tyr	Asp Thr Val Val Thr	Leu Lys Asn Met Ala	
	100	105 110	
tct cat ccc gtt agt	ctt cac gct gtc ggc	gtc tcc ttc tgg aaa tct	384
Ser His Pro Val Ser	Leu His Ala Val Gly	Val Ser Phe Trp Lys Ser	
	115	120 125	
tcc gaa ggc gct gaa	tat gag gat cac acc	agc caa agg gag aag gaa	432
Ser Glu Gly Ala Glu	Tyr Glu Asp His Thr	Ser Gln Arg Glu Lys Glu	
	130	135 140	
gac gat aaa gtc ctt	ccc ggt aaa agc caa	acc tac gtc tgg cag gtc	480
Asp Asp Lys Val Leu	Pro Gly Lys Ser Gln	Thr Tyr Val Trp Gln Val	
	145	150 155 160	
ctg aaa gaa aat ggt	cca aca gcc tct gac	cca cca tgt ctt acc tac	528
Leu Lys Glu Asn Gly	Pro Thr Ala Ser Asp	Pro Pro Cys Leu Thr Tyr	
	165	170 175	
tca tac ctg tct cac	gtg gac ctg gtg aaa	gac ctg aat tcg ggc ctc	576
Ser Tyr Leu Ser His	Val Asp Leu Val Lys	Asp Leu Asn Ser Gly Leu	
	180	185 190	
att gga gcc ctg ctg	gtt tgt aga gaa ggg	agt ctg acc aga gaa agg	624
Ile Gly Ala Leu Leu	Val Cys Arg Glu Gly	Ser Leu Thr Arg Glu Arg	
	195	200 205	
acc cag aac ctg cac	gaa ttt gta cta ctt	ttt gct gtc ttt gat gaa	672
Thr Gln Asn Leu His	Glu Phe Val Leu Leu	Phe Ala Val Phe Asp Glu	
	210	215 220	
ggg aaa agt tgg cac	tca gca aga aat gac	tcc tgg aca cgg gcc atg	720
Gly Lys Ser Trp His	Ser Ala Arg Asn Asp	Ser Trp Thr Arg Ala Met	
	225	230 235 240	
gat ccc gca cct gcc	agg gcc cag cct gca	atg cac aca gtc aat ggc	768
Asp Pro Ala Pro Ala	Arg Ala Gln Pro Ala	Met His Thr Val Asn Gly	
	245	250 255	
tat gtc aac agg tct	ctg cca ggt ctg atc	gga tgt cat aag aaa tca	816
Tyr Val Asn Arg Ser	Leu Pro Gly Leu Ile	Gly Cys His Lys Lys Ser	
	260	265 270	
gtc tac tgg cac gtg	att gga atg ggc acc	agc ccg gaa gtg cac tcc	864
Val Tyr Trp His Val	Ile Gly Met Gly Thr	Ser Pro Glu Val His Ser	
	275	280 285	
att ttt ctt gaa ggc	cac acg ttt ctc gtg	agg cac cat cgc cag gct	912
Ile Phe Leu Glu Gly	His Thr Phe Leu Val	Arg His His Arg Gln Ala	
	290	295 300	
tcc ttg gag atc tcg	cca cta act ttc ctc	act gct cag aca ttc ctg	960
Ser Leu Glu Ile Ser	Pro Leu Thr Phe Leu	Thr Ala Gln Thr Phe Leu	
	305	310 315 320	

atg gac ctt ggc cag ttc cta ctg ttt tgt cat atc tct tcc cac cac	1008
Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His	
325 330 335	
cat ggt ggc atg gag gct cac gtc aga gta gaa agc tgc gcc gag gag	1056
His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu	
340 345 350	
ccc cag ctg cgg agg aaa gct gat gaa gag gaa gat tat gat gac aat	1104
Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Glu Asp Tyr Asp Asp Asn	
355 360 365	
ttg tac gac tcg gac atg gac gtg gtc cgg ctc gat ggt gac gac gtg	1152
Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val	
370 375 380	
tct ccc ttt atc caa atc cgc tcg gtt gcc aag aag cat ccc aaa acc	1200
Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr	
385 390 395 400	
tgg gtg cac tac atc tct gca gag gag gag gac tgg gac tac gcc ccc	1248
Trp Val His Tyr Ile Ser Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro	
405 410 415	
gcg gtc ccc agc ccc agt gac aga agt tat aaa agt ctc tac ttg aac	1296
Ala Val Pro Ser Pro Ser Asp Arg Ser Tyr Lys Ser Leu Tyr Leu Asn	
420 425 430	
agt ggt cct cag cga att ggt agg aaa tac aaa aaa gct cga ttc gtc	1344
Ser Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Ala Arg Phe Val	
435 440 445	
gct tac acg gat gta aca ttt aag act cgt aaa gct att ccg tat gaa	1392
Ala Tyr Thr Asp Val Thr Phe Lys Thr Arg Lys Ala Ile Pro Tyr Glu	
450 455 460	
tca gga atc ctg gga cct tta ctt tat gga gaa gtt gga gac aca ctt	1440
Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu	
465 470 475 480	
ttg att ata ttt aag aat aaa gcg agc cga cca tat aac atc tac cct	1488
Leu Ile Ile Phe Lys Asn Lys Ala Ser Arg Pro Tyr Asn Ile Tyr Pro	
485 490 495	
cat gga atc act gat gtc agc gct ttg cac cca ggg aga ctt cta aaa	1536
His Gly Ile Thr Asp Val Ser Ala Leu His Pro Gly Arg Leu Leu Lys	
500 505 510	
ggt tgg aaa cat ttg aaa gac atg cca att ctg cca gga gag act ttc	1584
Gly Trp Lys His Leu Lys Asp Met Pro Ile Leu Pro Gly Glu Thr Phe	
515 520 525	
aag tat aaa tgg aca gtg act gtg gaa gat ggg cca acc aag tcc gat	1632
Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp	
530 535 540	
cct cgg tgc ctg acc cgc tac tac tcg agc tcc att aat cta gag aaa	1680
Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Ile Asn Leu Glu Lys	
545 550 555 560	
gat ctg gct tcg gga ctc att ggc cct ctc ctc atc tgc tac aaa gaa	1728
Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu	
565 570 575	
tct gta gac caa aga gga aac cag atg atg tca gac aag aga aac gtc	1776
Ser Val Asp Gln Arg Gly Asn Gln Met Met Ser Asp Lys Arg Asn Val	



tcc ccc cgg gcg cta aga aac agg gct cag aac gga gag gtg cct cgg	2592
Ser Pro Arg Ala Leu Arg Asn Arg Ala Gln Asn Gly Glu Val Pro Arg	
850 855 860	
ttc aag aag gtg gtc ttc cgg gaa ttt gct gac ggc tcc ttc acg cag	2640
Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln	
865 870 875 880	
ccg tcg tac cgc ggg gaa ctc aac aaa cac ttg ggg ctc ttg gga ccc	2688
Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu Gly Leu Leu Gly Pro	
885 890 895	
tac atc aga gcg gaa gtt gaa gac aac atc atg gta act ttc aaa aac	2736
Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Lys Asn	
900 905 910	
cag gcg tct cgt ccc tat tcc ttc tac tcg agc ctt att tct tat ccg	2784
Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro	
915 920 925	
gat gat cag gag caa ggg gca gaa cct cga cac aac ttc gtc cag cca	2832
Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn Phe Val Gln Pro	
930 935 940	
aat gaa acc aga act tac ttt tgg aaa gtg cag cat cac atg gca ccc	2880
Asn Glu Thr Arg Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro	
945 950 955 960	
aca gaa gac gag ttt gac tgc aaa gcc tgg gcc tac ttt tct gat gtt	2928
Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val	
965 970 975	
gac ctg gaa aaa gat gtg cac tca ggc ttg atc ggc ccc ctt ctg atc	2976
Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile	
980 985 990	
tgc cgc gcc aac acc ctg aac gct gct cac ggt aga caa gtg acc gtg	3024
Cys Arg Ala Asn Thr Leu Asn Ala Ala His Gly Arg Gln Val Thr Val	
995 1000 1005	
caa gaa ttt gct ctg ttt ttc act att ttt gat gag aca aag agc tgg	3072
Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp	
1010 1015 1020	
tac ttc act gaa aat gtg gaa agg aac tgc cgg gcc ccc tgc cat ctg	3120
Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu	
1025 1030 1035 1040	
cag atg gag gac ccc act ctg aaa gaa aac tat cgc ttc cat gca atc	3168
Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile	
1045 1050 1055	
aat ggc tat gtg atg gat aca ctc cct ggc tta gta atg gct cag aat	3216
Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn	
1060 1065 1070	
caa agg atc cga tgg tat ctg ctc agc atg ggc agc aat gaa aat atc	3264
Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile	
1075 1080 1085	
cat tcg att cat ttt agc gga cac gtg ttc agt gta cgg aaa aag gag	3312
His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu	
1090 1095 1100	
gag tat aaa atg gcc gtg tac aat ctc tat ccg ggt gtc ttt gag aca	3360
Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr	



1105	1110	1115	1120	
gtg gaa atg cta ccg tcc aaa gtt gga att tgg cga ata gaa tgc ctg				3408
Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu	1125	1130	1135	
att ggc gag cac ctg caa gct ggg atg agc acg act ttc ctg gtg tac				3456
Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr	1140	1145	1150	
agc aag aag tgt cag act ccc ctg gga atg gct tct gga cac att aga				3504
Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg	1155	1160	1165	
gat ttt cag att aca gct tca gga caa tat gga cag tgg gcc cca aag				3552
Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys	1170	1175	1180	
ctg gcc aga ctt cat tat tcc gga tca atc aat gcc tgg agc acc aag				3600
Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys	1185	1190	1195	1200
gag ccc ttt tct tgg atc aag gtg gat ctg ttg gca cca atg att att				3648
Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile	1205	1210	1215	
cac ggc atc aag acc cag ggt gcc cgt cag aag ttc tcc agc ctc tac				3696
His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr	1220	1225	1230	
atc tct cag ttt atc atc atg tat agt ctt gat ggg aag aag tgg cag				3744
Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln	1235	1240	1245	
act tat cga gga aat tcc act gga acc tta atg gtc ttc ttt ggc aat				3792
Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn	1250	1255	1260	
gtg gat tca tct ggg ata aaa cac aat att ttt aac cct cca att att				3840
Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile	1265	1270	1275	1280
gct cga tac atc cgt ttg cac cca act cat tat agc att cgc agc act				3888
Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr	1285	1290	1295	
ctt cgc atg gag ttg atg ggc tgt gat tta aat agt tgc agc atg cca				3936
Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro	1300	1305	1310	
ttg gga atg gag agt aaa gca ata tca gat gca cag att act gct tca				3984
Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser	1315	1320	1325	
tcc tac ttt acc aat atg ttt gcc acc tgg tct cct tca aaa gct cga				4032
Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg	1330	1335	1340	
ctt cac ctc caa ggg agg agt aat gcc tgg aga cct cag gtg aat aat				4080
Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn	1345	1350	1355	1360
cca aaa gag tgg ctg caa gtg gac ttc cag aag aca atg aaa gtc aca				4128
Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr	1365	1370	1375	

gga gta act act cag gga gta aaa tct ctg ctt acc agc atg tat gtg 4176  
 Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val  
 1380 1385 1390  
 aag gag ttc ctc atc tcc agc agt caa gat ggc cat cag tgg act ctc 4224  
 Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu  
 1395 1400 1405  
 ttt ttt cag aat ggc aaa gta aag gtt ttt cag gga aat caa gac tcc 4272  
 Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser  
 1410 1415 1420  
 ttc aca cct gtg gtg aac tct cta gac cca ccg tta ctg act cgc tac 4320  
 Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr  
 1425 1430 1435 1440  
 ctt cga att cac ccc cag agt tgg gtg cac cag att gcc ctg agg atg 4368  
 Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met  
 1445 1450 1455  
 gag gtt ctg ggc tgc gag gca cag gac ctc tac 4401  
 Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr  
 1460 1465

<210> 15  
 <211> 1467  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> HP44/OL-- factor VIII having the following  
 domains: Alp-A2p-app-A3p-Clh-C2h

<400> 15  
 Met Gln Leu Glu Leu Ser Thr Cys Val Phe Leu Cys Leu Leu Pro Leu  
 1 5 10 15  
 Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser  
 20 25 30  
 Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr  
 35 40 45  
 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val  
 50 55 60  
 Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser  
 65 70 75 80  
 Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile  
 85 90 95  
 Gln Ala Glu Val Tyr Asp Thr Val Val Thr Leu Lys Asn Met Ala  
 100 105 110  
 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser  
 115 120 125  
 Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu  
 130 135 140  
 Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val  
 145 150 155 160  
 Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr  
 165 170 175  
 Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu  
 180 185 190  
 Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg  
 195 200 205  
 Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu  
 210 215 220  
 Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met  
 225 230 235 240  
 Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly

59

770		775		780
Ile Ser Leu Pro Thr Phe	Gln Pro Glu Glu Asp Lys Met Asp Tyr Asp			
785		790		800
Asp Ile Phe Ser Thr Glu Thr Lys Gly Glu Asp Phe Asp Ile Tyr Gly		795		
		805		815
Glu Asp Glu Asn Gln Asp Pro Arg Ser Phe Gln Lys Arg Thr Arg His		810		
		820		830
Tyr Phe Ile Ala Ala Val Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu		825		
		835		845
Ser Pro Arg Ala Leu Arg Asn Arg Ala Gln Asn Gly Glu Val Pro Arg		840		
		850		860
Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln		855		
		865		875
Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu Gly Leu Leu Gly Pro		870		880
		885		895
Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Lys Asn		890		
		900		910
Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro		905		
		915		925
Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn Phe Val Gln Pro		920		
		930		940
Asn Glu Thr Arg Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro		935		
		945		955
Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val		950		960
		965		975
Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile		970		
		980		990
Cys Arg Ala Asn Thr Leu Asn Ala Ala His Gly Arg Gln Val Thr Val		985		
		995		1005
Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp		1000		
		1010		1020
Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu		1015		
		1025		1035
Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile		1030		1040
		1045		1055
Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn		1050		
		1060		1070
Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile		1065		
		1075		1085
His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu		1080		
		1090		1100
Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr		1095		
		1105		1115
Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu		1110		1120
		1125		1135
Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr		1130		
		1140		1150
Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg		1145		
		1155		1165
Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys		1160		
		1170		1180
Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys		1175		
		1185		1195
Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile		1190		1200
		1205		1215
His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr		1210		
		1220		1230
Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln		1225		
		1235		1245
Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn		1240		
		1250		1260
Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile		1255		
		1265		1275
Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr		1270		1280
		1285		1295
Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro		1290		

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      1300      1305      1310
Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser
      1315      1320      1325
Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg
      1330      1335      1340
Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn
1345      1350      1355      1360
Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr
      1365      1370      1375
Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val
      1380      1385      1390
Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu
      1395      1400      1405
Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser
      1410      1415      1420
Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr
1425      1430      1435      1440
Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met
      1445      1450      1455
Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr
      1460      1465

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<210> 16  
 <211> 4371  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> hybrid human and porcine factor VIII sequence

<221> CDS  
 <222> (1)...(4371)  
 <223> HP46/SQ-- factor VIII having the following  
 domains: Alp-A2h-aph-A3h-C1h-C2h

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ggc ttt agt gcc atc agg aga tac tac ctg ggc gca gtg gaa ctg tcc   96
Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
             20             25             30

tgg gac tac cgg caa agt gaa ctc ctc cgt gag ctg cac gtg gac acc   144
Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
             35             40             45

aga ttt cct gct aca gcg cca gga gct ctt ccg ttg ggc ccg tca gtc   192
Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
             50             55             60

ctg tac aaa aag act gtg ttc gta gag ttc acg gat caa ctt ttc agc   240
Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
             65             70             75             80

gtt gcc agg ccc agg cca cca tgg atg ggt ctg ctg ggt cct acc atc   288
Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
             85             90             95

cag gct gag gtt tac gac acg gtg gtc gtt acc ctg aag aac atg gct   336
Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
             100            105            110

tct cat ccc gtt agt ctt cac gct gtc ggc gtc tcc ttc tgg aaa tct   384

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Ser	His	Pro	Val	Ser	Leu	His	Ala	Val	Gly	Val	Ser	Phe	Trp	Lys	Ser		
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Ser	Glu	Gly	Ala	Glu	Tyr	Glu	Asp	His	Thr	Ser	Gln	Arg	Glu	Lys	Glu		
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Asp	Asp	Lys	Val	Leu	Pro	Gly	Lys	Ser	Gln	Thr	Tyr	Val	Trp	Gln	Val		
	145				150					155					160		
ctg	aaa	gaa	aat	ggg	cca	aca	gcc	tct	gac	cca	cca	tgt	ctt	acc	tac	528	
Leu	Lys	Glu	Asn	Gly	Pro	Thr	Ala	Ser	Asp	Pro	Pro	Cys	Leu	Thr	Tyr		
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tca	tac	ctg	tct	cac	gtg	gac	ctg	gtg	aaa	gac	ctg	aat	tcg	ggc	ctc	576	
Ser	Tyr	Leu		His	Val	Asp	Leu	Val	Lys	Asp	Leu	Asn	Ser	Gly	Leu		
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att	gga	gcc	ctg	ctg	gtt	tgt	aga	gaa	ggg	agt	ctg	acc	aga	gaa	agg	624	
Ile	Gly	Ala	Leu	Leu	Val	Cys	Arg	Glu	Gly	Ser	Leu	Thr	Arg	Glu	Arg		
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acc	cag	aac	ctg	cac	gaa	ttt	gta	cta	ctt	ttt	gct	gtc	ttt	gat	gaa	672	
Thr	Gln	Asn	Leu	His	Glu	Phe	Val	Leu	Leu	Phe	Ala	Val	Phe	Asp	Glu		
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Gly	Lys	Ser	Trp	His	Ser	Ala	Arg	Asn	Asp	Ser	Trp	Thr	Arg	Ala	Met		
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gat	ccc	gca	cct	gcc	agg	gcc	cag	cct	gca	atg	cac	aca	gtc	aat	ggc	768	
Asp	Pro	Ala	Pro	Ala	Arg	Ala	Gln	Pro	Ala	Met	His	Thr	Val	Asn	Gly		
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tat	gtc	aac	agg	tct	ctg	cca	ggg	ctg	atc	gga	tgt	cat	aag	aaa	tca	816	
Tyr	Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Lys	Lys	Ser		
			260					265					270				
gtc	tac	tgg	cac	gtg	att	gga	atg	ggc	acc	agc	ccg	gaa	gtg	cac	tcc	864	
Val	Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Ser	Pro	Glu	Val	His	Ser		
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Ile	Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	His	His	Arg	Gln	Ala		
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Ser	Leu	Glu	Ile	Ser	Pro	Leu	Thr	Phe	Leu	Thr	Ala	Gln	Thr	Phe	Leu		
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atg	gac	ctt	ggc	cag	ttc	cta	ctg	ttt	tgt	cat	atc	tct	tcc	cac	cac	1008	
Met	Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	His		
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cat	ggg	ggc	atg	gag	gct	cac	gtc	aga	gta	gaa	agc	tgc	gcc	gag	gag	1056	
His	Gly	Gly	Met	Glu	Ala	His	Val	Arg	Val	Glu	Ser	Cys	Ala	Glu	Glu		
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Pro	Gln	Leu	Arg	Arg	Lys	Ala	Asp	Glu	Glu	Glu	Asp	Tyr	Asp	Asp	Asn		
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Leu	Tyr	Asp	Ser	Asp	Met	Asp	Val	Val	Arg	Leu	Asp	Gly	Asp	Asp	Val		
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Trp Val His Tyr Ile Ala Ala Glu Glu Asp Trp Asp Tyr Ala Pro	
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Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn	
420 425 430	
aatggc cct cag cgg att ggt agg aag tac aaa aaa gtc cga ttt atg	1344
Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met	
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Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu	
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Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu	
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Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro	
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cacgga atc act gat gtc cgt cct ttg tat tca agg aga tta cca aaa	1536
His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys	
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Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe	
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Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp	
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ccgcgg tgc ctg acc cgc tat tac tct agt ttc gtt aat atg gag aga	1680
Pro Arg Cys Leu Thr Arg Tyr Ser Ser Phe Val Asn Met Glu Arg	
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Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu	
565 570 575	
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Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val	
580 585 590	
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Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu	
595 600 605	
aatata caa cgc ttt ctc ccc aat cca gct gga gtg cag ctt gag gat	1872
Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp	
610 615 620	
ccagag ttc caa gcc tcc aac atc atg cac agc atc aat ggc tat gtt	1920
Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val	
625 630 635 640	
tttgat agt ttg cag ttg tca gtt tgt ttg cat gag gtg gca tac tgg	1968

Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp	
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Tyr	Ile	Leu	Ser	Ile	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe	
			660					665					670			
tct	gga	tat	acc	ttc	aaa	cac	aaa	atg	gtc	tat	gaa	gac	aca	ctc	acc	2064
Ser	Gly	Tyr	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr	
		675					680					685				
cta	ttc	cca	ttc	tca	gga	gaa	act	gtc	ttc	atg	tcg	atg	gaa	aac	cca	2112
Leu	Phe	Pro	Phe	Ser	Gly	Glu	Thr	Val	Phe	Met	Ser	Met	Glu	Asn	Pro	
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ggg	cta	tgg	att	ctg	ggg	tgc	cac	aac	tca	gac	ttt	cgg	aac	aga	ggc	2160
Gly	Leu	Trp	Ile	Leu		Cys	His	Asn	Ser	Asp	Phe	Arg	Asn	Arg	Gly	
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Met	Thr	Ala	Leu	Leu	Lys	Val	Ser	Ser	Cys	Asp	Lys	Asn	Thr	Gly	Asp	
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Tyr	Tyr	Glu	Asp	Ser	Tyr	Glu	Asp	Ile	Ser	Ala	Tyr	Leu	Leu	Ser	Lys	
			740					745					750			
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Asn	Asn	Ala	Ile	Glu	Pro	Arg	Ser	Phe	Ser	Gln	Asn	Pro	Pro	Val	Leu	
		755					760					765				
aaa	cgc	cat	caa	cgg	gaa	ata	act	cgt	act	act	ctt	cag	tca	gat	caa	2352
Lys	Arg	His	Gln	Arg	Glu	Ile	Thr	Arg	Thr	Thr	Leu	Gln	Ser	Asp	Gln	
	770					775					780					
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Glu	Glu	Ile	Asp	Tyr	Asp	Asp	Thr	Ile	Ser	Val	Glu	Met	Lys	Lys	Glu	
785					790					795					800	
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Asp	Phe	Asp	Ile	Tyr	Asp	Glu	Asp	Glu	Asn	Gln	Ser	Pro	Arg	Ser	Phe	
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Gln	Lys	Lys	Thr	Arg	His	Tyr	Phe	Ile	Ala	Ala	Val	Glu	Arg	Leu	Trp	
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gat	tat	ggg	atg	agt	agc	tcc	cca	cat	gtt	cta	aga	aac	agg	gct	cag	2544
Asp	Tyr	Gly	Met	Ser	Ser	Ser	Pro	His	Val	Leu	Arg	Asn	Arg	Ala	Gln	
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Ser	Gly	Ser	Val	Pro	Gln	Phe	Lys	Lys	Val	Val	Phe	Gln	Glu	Phe	Thr	
	850					855					860					
gat	ggc	tcc	ttt	act	cag	ccc	tta	tac	cgt	gga	gaa	cta	aat	gaa	cat	2640
Asp	Gly	Ser	Phe	Thr	Gln	Pro	Leu	Tyr	Arg	Gly	Glu	Leu	Asn	Glu	His	
	865				870					875					880	
ttg	gga	ctc	ctg	ggg	cca	tat	ata	aga	gca	gaa	gtt	gaa	gat	aat	atc	2688
Leu	Gly	Leu	Leu	Gly	Pro	Tyr	Ile	Arg	Ala	Glu	Val	Glu	Asp	Asn	Ile	
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atg	gta	act	ttc	aga	aat	cag	gcc	tct	cgt	ccc	tat	tcc	ttc	tat	tct	2736
Met	Val	Thr	Phe	Arg	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser	
			900					905						910		



agc ctt att tct tat gag gaa gat cag agg caa gga gca gaa cct aga	2784
Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg	
915 920 925	
aaa aac ttt gtc aag cct aat gaa acc aaa act tac ttt tgg aaa gtg	2832
Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val	
930 935 940	
caa cat cat atg gca ccc act aaa gat gag ttt gac tgc aaa gcc tgg	2880
Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp	
945 950 955 960	
gct tat ttc tct gat gtt gac ctg gaa aaa gat gtg cac tca ggc ctg	2928
Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu	
965 970 975	
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Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His	
980 985 990	
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Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe	
995 1000 1005	
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Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys	
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agg gct ccc tgc aat atc cag atg gaa gat ccc act ttt aaa gag aat	3120
Arg Ala Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn	
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tat cgc ttc cat gca atc aat ggc tac ata atg gat aca cta cct ggc	3168
Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly	
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Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met	
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Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe	
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act gta cga aaa aaa gag gag tat aaa atg gca ctg tac aat ctc tat	3312
Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr	
1090 1095 1100	
cca ggt gtt ttt gag aca gtg gaa atg tta cca tcc aaa gct gga att	3360
Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile	
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Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser	
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Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met	
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Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr	
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Gly	Gln	Trp	Ala	Pro	Lys	Leu	Ala	Arg	Leu	His	Tyr	Ser	Gly	Ser	Ile		
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Leu	Ala	Pro	Met	Ile	Ile	His	Gly	Ile	Lys	Thr	Gln	Gly	Ala	Arg	Gln		
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Lys	Phe	Ser	Ser	Leu	Tyr	Ile	Ser	Gln	Phe	Ile	Ile	Met	Tyr	Ser	Leu		
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Asp	Gly	Lys	Lys	Trp	Gln	Thr	Tyr	Arg	Gly	Asn	Ser	Thr	Gly	Thr	Leu		
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Asn	Ser	Cys	Ser	Met	Pro	Leu	Gly	Met	Glu	Ser	Lys	Ala	Ile	Ser	Asp		
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Arg	Pro	Gln	Val	Asn	Asn	Pro	Lys	Glu	Trp	Leu	Gln	Val	Asp	Phe	Gln		
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Lys	Thr	Met	Lys	Val	Thr	Gly	Val	Thr	Thr	Gln	Gly	Val	Lys	Ser	Leu		
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Gln	Gly	Asn	Gln	Asp	Ser	Phe	Thr	Pro	Val	Val	Asn	Ser	Leu	Asp	Pro		
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Pro	Leu	Leu	Thr	Arg	Tyr	Leu	Arg	Ile	His	Pro	Gln	Ser	Trp	Val	His		
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cag att gcc ctg agg atg gag gtt ctg ggc tgc gag gca cag gac ctg 4368  
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tac 4371  
 Tyr

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 Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser  
           20                  25                  30  
 Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr  
           35                  40                  45  
 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val  
           50                  55                  60  
 Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser  
   65                  70                  75                  80  
 Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile  
           85                  90                  95  
 Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala  
           100                  105                  110  
 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser  
           115                  120                  125  
 Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu  
   130                  135                  140  
 Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val  
   145                  150                  155                  160  
 Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr  
           165                  170                  175  
 Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu  
           180                  185                  190  
 Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg  
           195                  200                  205  
 Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu  
   210                  215                  220  
 Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met  
   225                  230                  235                  240  
 Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly  
           245                  250                  255  
 Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser  
           260                  265                  270  
 Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser  
           275                  280                  285  
 Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala  
   290                  295                  300  
 Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu  
   305                  310                  315                  320  
 Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His  
           325                  330                  335  
 His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu  
           340                  345                  350  
 Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Glu Asp Tyr Asp Asp Asn  
           355                  360                  365

Leu	Tyr	Asp	Ser	Asp	Met	Asp	Val	Val	Arg	Leu	Asp	Gly	Asp	Asp	Val
370						375				380					
Ser	Pro	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr
385					390					395					400
Trp	Val	His	Tyr	Ile	Ala	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro
				405					410					415	
Leu	Val	Leu	Ala	Pro	Asp	Asp	Arg	Ser	Tyr	Lys	Ser	Gln	Tyr	Leu	Asn
			420				425						430		
Asn	Gly	Pro	Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Val	Arg	Phe	Met
		435				440						445			
Ala	Tyr	Thr	Asp	Glu	Thr	Phe	Lys	Thr	Arg	Glu	Ala	Ile	Gln	His	Glu
	450					455					460				
Ser	Gly	Ile	Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	Val	Gly	Asp	Thr	Leu
465					470					475					480
Leu	Ile	Ile	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro
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His	Gly	Ile	Thr	Asp	Val	Arg	Pro	Leu	Tyr	Ser	Arg	Arg	Leu	Pro	Lys
			500					505					510		
Gly	Val	Lys	His	Leu	Lys	Asp	Phe	Pro	Ile	Leu	Pro	Gly	Glu	Ile	Phe
		515					520					525			
Lys	Tyr	Lys	Trp	Thr	Val	Thr	Val	Glu	Asp	Gly	Pro	Thr	Lys	Ser	Asp
	530					535					540				
Pro	Arg	Cys	Leu	Thr	Arg	Tyr	Tyr	Ser	Ser	Phe	Val	Asn	Met	Glu	Arg
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Asp	Leu	Ala	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Tyr	Lys	Glu
				565				570						575	
Ser	Val	Asp	Gln	Arg	Gly	Asn	Gln	Ile	Met	Ser	Asp	Lys	Arg	Asn	Val
			580				585						590		
Ile	Leu	Phe	Ser	Val	Phe	Asp	Glu	Asn	Arg	Ser	Trp	Tyr	Leu	Thr	Glu
		595				600						605			
Asn	Ile	Gln	Arg	Phe	Leu	Pro	Asn	Pro	Ala	Gly	Val	Gln	Leu	Glu	Asp
	610					615					620				
Pro	Glu	Phe	Gln	Ala	Ser	Asn	Ile	Met	His	Ser	Ile	Asn	Gly	Tyr	Val
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Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp
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Tyr	Ile	Leu	Ser	Ile	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe
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Ser	Gly	Tyr	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr
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Gly	Leu	Trp	Ile	Leu	Gly	Cys	His	Asn	Ser	Asp	Phe	Arg	Asn	Arg	Gly
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Met	Thr	Ala	Leu	Leu	Lys	Val	Ser	Ser	Cys	Asp	Lys	Asn	Thr	Gly	Asp
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Tyr	Tyr	Glu	Asp	Ser	Tyr	Glu	Asp	Ile	Ser	Ala	Tyr	Leu	Leu	Ser	Lys
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Asn	Asn	Ala	Ile	Glu	Pro	Arg	Ser	Phe	Ser	Gln	Asn	Pro	Pro	Val	Leu
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Lys	Arg	His	Gln	Arg	Glu	Ile	Thr	Arg	Thr	Thr	Leu	Gln	Ser	Asp	Gln
	770					775					780				
Glu	Glu	Ile	Asp	Tyr	Asp	Asp	Thr	Ile	Ser	Val	Glu	Met	Lys	Lys	Glu
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Asp	Phe	Asp	Ile	Tyr	Asp	Glu	Asp	Glu	Asn	Gln	Ser	Pro	Arg	Ser	Phe
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Gln	Lys	Lys	Thr	Arg	His	Tyr	Phe	Ile	Ala	Ala	Val	Glu	Arg	Leu	Trp
			820				825						830		
Asp	Tyr	Gly	Met	Ser	Ser	Ser	Pro	His	Val	Leu	Arg	Asn	Arg	Ala	Gln
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Ser	Gly	Ser	Val	Pro	Gln	Phe	Lys	Lys	Val	Val	Phe	Gln	Glu	Phe	Thr
	850					855					860				
Asp	Gly	Ser	Phe	Thr	Gln	Pro	Leu	Tyr	Arg	Gly	Glu	Leu	Asn	Glu	His
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Leu	Gly	Leu	Leu	Gly	Pro	Tyr	Ile	Arg	Ala	Glu	Val	Glu	Asp	Asn	Ile
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Met	Val	Thr	Phe	Arg	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser	
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Ser	Leu	Ile	Ser	Tyr	Glu	Glu	Asp	Gln	Arg	Gln	Gly	Ala	Glu	Pro	Arg	
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Lys	Asn	Phe	Val	Lys	Pro	Asn	Glu	Thr	Lys	Thr	Tyr	Phe	Trp	Lys	Val	
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Gln	His	His	Met	Ala	Pro	Thr	Lys	Asp	Glu	Phe	Asp	Cys	Lys	Ala	Trp	
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Ala	Tyr	Phe	Ser	Asp	Val	Asp	Leu	Glu	Lys	Asp	Val	His	Ser	Gly	Leu	
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Ile	Gly	Pro	Leu	Leu	Val	Cys	His	Thr	Asn	Thr	Leu	Asn	Pro	Ala	His	
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Gly	Arg	Gln	Val	Thr	Val	Gln	Glu	Phe	Ala	Leu	Phe	Phe	Thr	Ile	Phe	
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Asp	Glu	Thr	Lys	Ser	Trp	Tyr	Phe	Thr	Glu	Asn	Met	Glu	Arg	Asn	Cys	
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Arg	Ala	Pro	Cys	Asn	Ile	Gln	Met	Glu	Asp	Pro	Thr	Phe	Lys	Glu	Asn	
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Tyr	Arg	Phe	His	Ala	Ile	Asn	Gly	Tyr	Ile	Met	Asp	Thr	Leu	Pro	Gly	
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Leu	Val	Met	Ala	Gln	Asp	Gln	Arg	Ile	Arg	Trp	Tyr	Leu	Leu	Ser	Met	
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Gly	Ser	Asn	Glu	Asn	Ile	His	Ser	Ile	His	Phe	Ser	Gly	His	Val	Phe	
	1075						1080					1085				
Thr	Val	Arg	Lys	Lys	Glu	Glu	Tyr	Lys	Met	Ala	Leu	Tyr	Asn	Leu	Tyr	
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Pro	Gly	Val	Phe	Glu	Thr	Val	Glu	Met	Leu	Pro	Ser	Lys	Ala	Gly	Ile	
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Trp	Arg	Val	Glu	Cys	Leu	Ile	Gly	Glu	His	Leu	His	Ala	Gly	Met	Ser	
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Thr	Leu	Phe	Leu	Val	Tyr	Ser	Asn	Lys	Cys	Gln	Thr	Pro	Leu	Gly	Met	
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Ala	Ser	Gly	His	Ile	Arg	Asp	Phe	Gln	Ile	Thr	Ala	Ser	Gly	Gln	Tyr	
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Gly	Gln	Trp	Ala	Pro	Lys	Leu	Ala	Arg	Leu	His	Tyr	Ser	Gly	Ser	Ile	
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Asn	Ala	Trp	Ser	Thr	Lys	Glu	Pro	Phe	Ser	Trp	Ile	Lys	Val	Asp	Leu	
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Leu	Ala	Pro	Met	Ile	Ile	His	Gly	Ile	Lys	Thr	Gln	Gly	Ala	Arg	Gln	
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Lys	Phe	Ser	Ser	Leu	Tyr	Ile	Ser	Gln	Phe	Ile	Ile	Met	Tyr	Ser	Leu	
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Asp	Gly	Lys	Lys	Trp	Gln	Thr	Tyr	Arg	Gly	Asn	Ser	Thr	Gly	Thr	Leu	
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Met	Val	Phe	Phe	Gly	Asn	Val	Asp	Ser	Ser	Gly	Ile	Lys	His	Asn	Ile	
	1250					1255					1260					
Phe	Asn	Pro	Pro	Ile	Ile	Ala	Arg	Tyr	Ile	Arg	Leu	His	Pro	Thr	His	
1265					1270					1275					1280	
Tyr	Ser	Ile	Arg	Ser	Thr	Leu	Arg	Met	Glu	Leu	Met	Gly	Cys	Asp	Leu	
			1285						1290						1295	
Asn	Ser	Cys	Ser	Met	Pro	Leu	Gly	Met	Glu	Ser	Lys	Ala	Ile	Ser	Asp	
		1300						1305					1310			
Ala	Gln	Ile	Thr	Ala	Ser	Ser	Tyr	Phe	Thr	Asn	Met	Phe	Ala	Thr	Trp	
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Ser	Pro	Ser	Lys	Ala	Arg	Leu	His	Leu	Gln	Gly	Arg	Ser	Asn	Ala	Trp	
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Arg	Pro	Gln	Val	Asn	Asn	Pro	Lys	Glu	Trp	Leu	Gln	Val	Asp	Phe	Gln	
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Lys	Thr	Met	Lys	Val	Thr	Gly	Val	Thr	Thr	Gln	Gly	Val	Lys	Ser	Leu	
			1365						1370						1375	
Leu	Thr	Ser	Met	Tyr	Val	Lys	Glu	Phe	Leu	Ile	Ser	Ser	Ser	Gln	Asp	
		1380						1385					1390			
Gly	His	Gln	Trp	Thr	Leu	Phe	Phe	Gln	Asn	Gly	Lys	Val	Lys	Val	Phe	
	1395						1400					1405				
Gln	Gly	Asn	Gln	Asp	Ser	Phe	Thr	Pro	Val	Val	Asn	Ser	Leu	Asp	Pro	
	1410					1415						1420				

Pro Leu Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His  
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 Gln Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu  
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 Tyr

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 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> hybrid human and porcine factor VIII sequence

<221> CDS  
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 Met Gln Leu Glu Leu Ser Thr Cys Val Phe Leu Cys Leu Leu Pro Leu  
 1 5 10 15  
 ggc ttt agt gcc atc agg aga tac tac ctg ggc gca gtg gaa ctg tcc 96  
 Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser  
 20 25 30  
 tgg gac tac cgg caa agt gaa ctc ctc cgt gag ctg cac gtg gac acc 144  
 Trp Asp Tyr Arg Gln Ser Glu Leu Arg Glu Leu His Val Asp Thr  
 35 40 45  
 aga ttt cct gct aca gcg cca gga gct ctt ccg ttg ggc ccg tca gtc 192  
 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val  
 50 55 60  
 ctg tac aaa aag act gtg ttc gta gag ttc acg gat caa ctt ttc agc 240  
 Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser  
 65 70 75 80  
 gtt gcc agg ccc agg cca cca tgg atg ggt ctg ctg ggt cct acc atc 288  
 Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile  
 85 90 95  
 cag gct gag gtt tac gac acg gtg gtc gtt acc ctg aag aac atg gct 336  
 Gln Ala Glu Val Tyr Asp Thr Val Val Thr Leu Lys Asn Met Ala  
 100 105 110  
 tct cat ccc gtt agt ctt cac gct gtc ggc gtc tcc ttc tgg aaa tct 384  
 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser  
 115 120 125  
 tcc gaa ggc gct gaa tat gag gat cac acc agc caa agg gag aag gaa 432  
 Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu  
 130 135 140  
 gac gat aaa gtc ctt ccc ggt aaa agc caa acc tac gtc tgg cag gtc 480  
 Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val  
 145 150 155 160  
 ctg aaa gaa aat ggt cca aca gcc tct gac cca cca tgt ctt acc tac 528  
 Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr  
 165 170 175

tca tac ctg tct cac gtg gac ctg gtg aaa gac ctg aat tcg ggc ctc	576
Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu	
180 185 190	
att gga gcc ctg ctg gtt tgt aga gaa ggg agt ctg acc aga gaa agg	624
Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg	
195 200 205	
acc cag aac ctg cac gaa ttt gta cta ctt ttt gct gtc ttt gat gaa	672
Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu	
210 215 220	
ggg aaa agt tgg cac tca gca aga aat gac tcc tgg aca cgg gcc atg	720
Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met	
225 230 235 240	
gat ccc gca cct gcc agg gcc cag cct gca atg cac aca gtc aat ggc	768
Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly	
245 250 255	
tat gtc aac agg tct ctg cca ggt ctg atc gga tgt cat aag aaa tca	816
Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser	
260 265 270	
gtc tac tgg cac gtg att gga atg ggc acc agc ccg gaa gtg cac tcc	864
Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser	
275 280 285	
att ttt ctt gaa ggc cac acg ttt ctc gtg agg cac cat cgc cag gct	912
Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala	
290 295 300	
tcc ttg gag atc tcg cca cta act ttc ctc act gct cag aca ttc ctg	960
Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu	
305 310 315 320	
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Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His	
325 330 335	
cat ggt ggc atg gag gct cac gtc aga gta gaa agc tgc gcc gag gag	1056
His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu	
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ccc cag ctg cgg agg aaa gct gat gaa gag gaa gat tat gat gac aat	1104
Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Glu Asp Tyr Asp Asp Asn	
355 360 365	
ttg tac gac tcg gac atg gac gtg gtc cgg ctc gat ggt gac gac gtg	1152
Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val	
370 375 380	
tct ccc ttt atc caa atc cgc tca gtt gcc aag aag cat cct aaa act	1200
Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr	
385 390 395 400	
tgg gta cat tac att gct gct gaa gag gag gac tgg gac tat gct ccc	1248
Trp Val His Tyr Ile Ala Ala Glu Glu Asp Trp Asp Tyr Ala Pro	
405 410 415	
tta gtc ctc gcc ccc gat gac aga agt tat aaa agt caa tat ttg aac	1296
Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn	
420 425 430	
aat ggc cct cag cgg att ggt agg aag tac aaa aaa gtc cga ttt atg	1344
Asn Gly Pro Gln Arg Ile Gly Arg Lys Lys Lys Val Arg Phe Met	

435	440	445	
gca tac aca gat gaa acc ttt aag acg cgt gaa gct att cag cat gaa Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu 450 455 460			1392
tca gga atc ttg gga cct tta ctt tat ggg gaa gtt gga gac aca ctg Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu 465 470 475 480			1440
ttg att ata ttt aag aat caa gca agc aga cca tat aac atc tac cct Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro 485 490 495			1488
cac gga atc act gat gtc cgt cct ttg tat tca agg aga tta cca aaa His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys 500 505 510			1536
ggg gta aaa cat ttg aag gat ttt cca att ctg cca gga gaa ata ttc Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe 515 520 525			1584
aaa tat aaa tgg aca gtg act gta gaa gat ggg cca act aaa tca gat Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp 530 535 540			1632
ccg cgg tgc ctg acc cgc tat tac tct agt ttc gtt aat atg gag aga Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg 545 550 555 560			1680
gat cta gct tca gga ctc att ggc cct ctc ctc atc tgc tac aaa gaa Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu 565 570 575			1728
tct gta gat caa aga gga aac cag ata atg tca gac aag agg aat gtc Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val 580 585 590			1776
atc ctg ttt tct gta ttt gat gag aac cga agc tgg tac ctc aca gag Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu 595 600 605			1824
aat ata caa cgc ttt ctc ccc aat cca gct gga gtg cag ctt gag gat Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp 610 615 620			1872
cca gag ttc caa gcc tcc aac atc atg cac agc atc aat ggc tat gtt Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val 625 630 635 640			1920
ttt gat agt ttg cag ttg tca gtt tgt ttg cat gag gtg gca tac tgg Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp 645 650 655			1968
tac att cta agc att gga gca cag act gac ttc ctt tct gtc ttc ttc Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe 660 665 670			2016
tct gga tat acc ttc aaa cac aaa atg gtc tat gaa gac aca ctc acc Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr 675 680 685			2064
cta ttc cca ttc tca gga gaa act gtc ttc atg tcg atg gaa aac cca Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro 690 695 700			2112



ggc cta tgg att ctg ggg tgc cac aac tca gac ttt cgg aac aga ggc	2160
Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly	
705 710 715 720	
atg acc gcc tta ctg aag gtt tct agt tgt gac aag aac act ggt gat	2208
Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp	
725 730 735	
tat tac gag gac agt tat gaa gat att tca gca tac ttg ctg agt aaa	2256
Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys	
740 745 750	
aac aat gcc att gaa cct agg agc ttt gcc cag aat tca aga ccc cct	2304
Asn Asn Ala Ile Glu Pro Arg Ser Phe Ala Gln Asn Ser Arg Pro Pro	
755 760 765	
agt gcg agc gct cca aag cct ccg gtc ctg cga cgg cat cag agg gac	2352
Ser Ala Ser Ala Pro Lys Pro Pro Val Leu Arg Arg His Gln Arg Asp	
770 775 780	
ata agc ctt cct act ttt cag ccg gag gaa gac aaa atg gac tat gat	2400
Ile Ser Leu Pro Thr Phe Gln Pro Glu Glu Asp Lys Met Asp Tyr Asp	
785 790 795 800	
gat atc ttc tca act gaa acg aag gga gaa gat ttt gac att tac ggt	2448
Asp Ile Phe Ser Thr Glu Thr Lys Gly Glu Asp Phe Asp Ile Tyr Gly	
805 810 815	
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Glu Asp Glu Asn Gln Asp Pro Arg Ser Phe Gln Lys Arg Thr Arg His	
820 825 830	
tat ttc att gct gcg gtg gag cag ctc tgg gat tac ggg atg agc gaa	2544
Tyr Phe Ile Ala Ala Val Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu	
835 840 845	
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Ser Pro Arg Ala Leu Arg Asn Arg Ala Gln Asn Gly Glu Val Pro Arg	
850 855 860	
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Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln	
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Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu Gly Leu Leu Gly Pro	
885 890 895	
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Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Lys Asn	
900 905 910	
cag gcg tct cgt ccc tat tcc ttc tac tcg agc ctt att tct tat ccg	2784
Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro	
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Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn Phe Val Gln Pro	
930 935 940	
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Asn Glu Thr Arg Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro	
945 950 955 960	
aca gaa gac gag ttt gac tgc aaa gcc tgg gcc tac ttt tct gat gtt	2928
Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val	

965										970					975					
gac	ctg	gaa	aaa	gat	gtg	cac	tca	ggc	ttg	atc	ggc	ccc	ctt	ctg	atc	2976				
Asp	Leu	Glu	Lys	Asp	Val	His	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile					
			980					985					990							
tgc	cgc	gcc	aac	acc	ctg	aac	gct	gct	cac	ggg	aga	caa	gtg	acc	gtg	3024				
Cys	Arg	Ala	Asn	Thr	Leu	Asn	Ala	Ala	His	Gly	Arg	Gln	Val	Thr	Val					
			995				1000					1005								
caa	gaa	ttt	gct	ctg	ttt	ttc	act	att	ttt	gat	gag	aca	aag	agc	tgg	3072				
Gln	Glu	Phe	Ala	Leu	Phe	Phe	Thr	Ile	Phe	Asp	Glu	Thr	Lys	Ser	Trp					
			1010				1015				1020									
tac	ttc	act	gaa	aat	gtg	gaa	agg	aac	tgc	cgg	gcc	ccc	tgc	cat	ctg	3120				
Tyr	Phe	Thr	Glu	Asn	Val	Glu	Arg	Asn	Cys	Arg	Ala	Pro	Cys	His	Leu					
1025					1030					1035					1040					
cag	atg	gag	gac	ccc	act	ctg	aaa	gaa	aac	tat	cgc	ttc	cat	gca	atc	3168				
Gln	Met	Glu	Asp	Pro	Thr	Leu	Lys	Glu	Asn	Tyr	Arg	Phe	His	Ala	Ile					
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aat	ggc	tat	gtg	atg	gat	aca	ctc	cct	ggc	tta	gta	atg	gct	cag	aat	3216				
Asn	Gly	Tyr	Val	Met	Asp	Thr	Leu	Pro	Gly	Leu	Val	Met	Ala	Gln	Asn					
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caa	agg	atc	cga	tgg	tat	ctg	ctc	agc	atg	ggc	agc	aat	gaa	aat	atc	3264				
Gln	Arg	Ile	Arg	Trp	Tyr	Leu	Leu	Ser	Met	Gly	Ser	Asn	Glu	Asn	Ile					
			1075				1080				1085									
cat	tcg	att	cat	ttt	agc	gga	cac	gtg	ttc	agt	gta	cgg	aaa	aag	gag	3312				
His	Ser	Ile	His	Phe	Ser	Gly	His	Val	Phe	Ser	Val	Arg	Lys	Lys	Glu					
			1090				1095				1100									
gag	tat	aaa	atg	gcc	gtg	tac	aat	ctc	tat	ccg	ggg	gtc	ttt	gag	aca	3360				
Glu	Tyr	Lys	Met	Ala	Val	Tyr	Asn	Leu	Tyr	Pro	Gly	Val	Phe	Glu	Thr					
1105					1110					1115					1120					
gtg	gaa	atg	cta	ccg	tcc	aaa	gtt	gga	att	tgg	cga	ata	gaa	tgc	ctg	3408				
Val	Glu	Met	Leu	Pro	Ser	Lys	Val	Gly	Ile	Trp	Arg	Ile	Glu	Cys	Leu					
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att	ggc	gag	cac	ctg	caa	gct	ggg	atg	agc	acg	act	ttc	ctg	gtg	tac	3456				
Ile	Gly	Glu	His	Leu	Gln	Ala	Gly	Met	Ser	Thr	Thr	Phe	Leu	Val	Tyr					
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agc	aag	aag	tgt	cag	act	ccc	ctg	gga	atg	gct	tct	gga	cac	att	aga	3504				
Ser	Lys	Lys	Cys	Gln	Thr	Pro	Leu	Gly	Met	Ala	Ser	Gly	His	Ile	Arg					
			1155				1160				1165									
gat	ttt	cag	att	aca	gct	tca	gga	caa	tat	gga	cag	tgg	gcc	cca	aag	3552				
Asp	Phe	Gln	Ile	Thr	Ala	Ser	Gly	Gln	Tyr	Gly	Gln	Trp	Ala	Pro	Lys					
			1170				1175				1180									
ctg	gcc	aga	ctt	cat	tat	tcc	gga	tca	atc	aat	gcc	tgg	agc	acc	aag	3600				
Leu	Ala	Arg	Leu	His	Tyr	Ser	Gly	Ser	Ile	Asn	Ala	Trp	Ser	Thr	Lys					
1185					1190					1195					1200					
gag	ccc	ttt	tct	tgg	atc	aag	gtg	gat	ctg	ttg	gca	cca	atg	att	att	3648				
Glu	Pro	Phe	Ser	Trp	Ile	Lys	Val	Asp	Leu	Leu	Ala	Pro	Met	Ile	Ile					
			1205				1210				1215									
cac	ggc	atc	aag	acc	cag	ggg	gcc	cgt	cag	aag	ttc	tcc	agc	ctc	tac	3696				
His	Gly	Ile	Lys	Thr	Gln	Gly	Ala	Arg	Gln	Lys	Phe	Ser	Ser	Leu	Tyr					
			1220				1225				1230									

atc tct cag ttt atc atc atg tat agt ctt gat ggg aag aag tgg cag Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln 1235 1240 1245	3744
act tat cga gga aat tcc act gga acc tta atg gtc ttc ttt ggc aat Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn 1250 1255 1260	3792
gtg gat tca tct ggg ata aaa cac aat att ttt aac cct cca att att Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile 1265 1270 1275 1280	3840
gct cga tac atc cgt ttg cac cca act cat tat agc att cgc agc act Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr 1285 1290 1295	3888
ctt cgc atg gag ttg atg ggc tgt gat tta aat agt tgc agc atg cca Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro 1300 1305 1310	3936
ttg gga atg gag agt aaa gca ata tca gat gca cag att act gct tca Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser 1315 1320 1325	3984
tcc tac ttt acc aat atg ttt gcc acc tgg tct cct tca aaa gct cga Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg 1330 1335 1340	4032
ctt cac ctc caa ggg agg agt aat gcc tgg aga cct cag gtg aat aat Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn 1345 1350 1355 1360	4080
cca aaa gag tgg ctg caa gtg gac ttc cag aag aca atg aaa gtc aca Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr 1365 1370 1375	4128
gga gta act act cag gga gta aaa tct ctg ctt acc agc atg tat gtg Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val 1380 1385 1390	4176
aag gag ttc ctc atc tcc agc agt caa gat ggc cat cag tgg act ctc Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu 1395 1400 1405	4224
ttt ttt cag aat ggc aaa gta aag gtt ttt cag gga aat caa gac tcc Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser 1410 1415 1420	4272
ttc aca cct gtg gtg aac tct cta gac cca ccg tta ctg act cgc tac Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr 1425 1430 1435 1440	4320
ctt cga att cac ccc cag agt tgg gtg cac cag att gcc ctg agg atg Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met 1445 1450 1455	4368
gag gtt ctg ggc tgc gag gca cag gac ctc tac Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr 1460 1465	4401

<210> 19  
 <211> 1467  
 <212> PRT  
 <213> Artificial Sequence

<220>.

<223> HP47/OL -- factor VIII having the following  
domains: Alp-A2h-app-A3p-C1h-C2h

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			20					25					30		
Trp	Asp	Tyr	Arg	Gln	Ser	Glu	Leu	Leu	Arg	Glu	Leu	His	Val	Asp	Thr
		35					40					45			
Arg	Phe	Pro	Ala	Thr	Ala	Pro	Gly	Ala	Leu	Pro	Leu	Gly	Pro	Ser	Val
		50				55					60				
Leu	Tyr	Lys	Lys	Thr	Val	Phe	Val	Glu	Phe	Thr	Asp	Gln	Leu	Phe	Ser
65					70				75					80	
Val	Ala	Arg	Pro	Arg	Pro	Pro	Trp	Met	Gly	Leu	Leu	Gly	Pro	Thr	Ile
				85					90					95	
Gln	Ala	Glu	Val	Tyr	Asp	Thr	Val	Val	Val	Thr	Leu	Lys	Asn	Met	Ala
			100					105					110		
Ser	His	Pro	Val	Ser	Leu	His	Ala	Val	Gly	Val	Ser	Phe	Trp	Lys	Ser
		115					120					125			
Ser	Glu	Gly	Ala	Glu	Tyr	Glu	Asp	His	Thr	Ser	Gln	Arg	Glu	Lys	Glu
	130					135					140				
Asp	Asp	Lys	Val	Leu	Pro	Gly	Lys	Ser	Gln	Thr	Tyr	Val	Trp	Gln	Val
145					150				155					160	
Leu	Lys	Glu	Asn	Gly	Pro	Thr	Ala	Ser	Asp	Pro	Pro	Cys	Leu	Thr	Tyr
			165						170					175	
Ser	Tyr	Leu	Ser	His	Val	Asp	Leu	Val	Lys	Asp	Leu	Asn	Ser	Gly	Leu
		180					185					190			
Ile	Gly	Ala	Leu	Leu	Val	Cys	Arg	Glu	Gly	Ser	Leu	Thr	Arg	Glu	Arg
	195					200					205				
Thr	Gln	Asn	Leu	His	Glu	Phe	Val	Leu	Leu	Phe	Ala	Val	Phe	Asp	Glu
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Gly	Lys	Ser	Trp	His	Ser	Ala	Arg	Asn	Asp	Ser	Trp	Thr	Arg	Ala	Met
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Asp	Pro	Ala	Pro	Ala	Arg	Ala	Gln	Pro	Ala	Met	His	Thr	Val	Asn	Gly
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Tyr	Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Lys	Lys	Ser
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Val	Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Ser	Pro	Glu	Val	His	Ser
	275					280					285				
Ile	Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	His	His	Arg	Gln	Ala
	290					295					300				
Ser	Leu	Glu	Ile	Ser	Pro	Leu	Thr	Phe	Leu	Thr	Ala	Gln	Thr	Phe	Leu
305					310				315					320	
Met	Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	His
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His	Gly	Gly	Met	Glu	Ala	His	Val	Arg	Val	Glu	Ser	Cys	Ala	Glu	Glu
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Pro	Gln	Leu	Arg	Arg	Lys	Ala	Asp	Glu	Glu	Glu	Asp	Tyr	Asp	Asp	Asn
		355				360					365				
Leu	Tyr	Asp	Ser	Asp	Met	Asp	Val	Val	Arg	Leu	Asp	Gly	Asp	Asp	Val
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Ser	Pro	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr
385					390				395					400	
Trp	Val	His	Tyr	Ile	Ala	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro
				405					410					415	
Leu	Val	Leu	Ala	Pro	Asp	Asp	Arg	Ser	Tyr	Lys	Ser	Gln	Tyr	Leu	Asn
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Asn	Gly	Pro	Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Val	Arg	Phe	Met
		435				440					445				
Ala	Tyr	Thr	Asp	Glu	Thr	Phe	Lys	Thr	Arg	Glu	Ala	Ile	Gln	His	Glu
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Ser	Gly	Ile	Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	Val	Gly	Asp	Thr	Leu
465					470				475					480	
Leu	Ile	Ile	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro

77

1010		1015		1020
Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu				
1025		1030		1035
Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile				1040
	1045		1050	1055
Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn				
	1060		1065	1070
Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile				
	1075		1080	1085
His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu				
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Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr				
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Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu				1120
	1125		1130	1135
Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr				
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Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg				
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Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys				
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Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys				
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Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile				1200
	1205		1210	1215
His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr				
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Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln				
	1235		1240	1245
Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn				
	1250		1255	1260
Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile				
1265		1270		1275
Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr				
	1285		1290	1295
Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro				
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Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser				
	1315		1320	1325
Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg				
	1330		1335	1340
Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn				
1345		1350		1355
Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr				
	1365		1370	1375
Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val				
	1380		1385	1390
Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu				
	1395		1400	1405
Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser				
	1410		1415	1420
Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr				
1425		1430		1435
Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met				
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Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr				
	1460		1465	

<210> 20

<211> 4401

<212> DNA

<213> Artificial Sequence

<220>

<223> hybrid human and porcine factor VIII sequence

<221> CDS  
 <222> (1)...(4401)  
 <223> HP63/OL -- factor VIII variant

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ggc ttt agt gcc atc agg aga tac tac ctg ggc gca gtg gaa ctg tcc 96
Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
20 25 30

tgg gac tac cgg caa agt gaa ctc ctc cgt gag ctg cac gtg gac acc 144
Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
35 40 45

aga ttt cct gct aca gcg cca gga gct ctt ccg ttg ggc ccg tca gtc 192
Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
50 55 60

ctg tac aaa aag act gtg ttc gta gag ttc acg gat caa ctt ttc agc 240
Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
65 70 75 80

gtt gcc agg ccc agg cca cca tgg atg ggt ctg ctg ggt cct acc atc 288
Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
85 90 95

cag gct gag gtt tac gac acg gtg gtc gtt acc ctg aag aac atg gct 336
Gln Ala Glu Val Tyr Asp Thr Val Val Thr Leu Lys Asn Met Ala
100 105 110

tct cat ccc gtt agt ctt cac gct gtc ggc gtc tcc ttc tgg aaa tct 384
Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
115 120 125

tcc gaa ggc gct gaa tat gag gat cac acc agc caa agg gag aag gaa 432
Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
130 135 140

gac gat aaa gtc ctt ccc ggt aaa agc caa acc tac gtc tgg cag gtc 480
Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
145 150 155 160

ctg aaa gaa aat ggt cca aca gcc tct gac cca cca tgt ctt acc tac 528
Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
165 170 175

tca tac ctg tct cac gtg gac ctg gtg aaa gac ctg aat tcg ggc ctc 576
Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
180 185 190

att gga gcc ctg ctg gtt tgt aga gaa ggg agt ctg acc aga gaa agg 624
Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg
195 200 205

acc cag aac ctg cac gaa ttt gta cta ctt ttt gct gtc ttt gat gaa 672
Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
210 215 220

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Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met
225 230 235 240

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tat gtc aac agg tct ctg cca ggt ctg atc gga tgt cat aag aaa tca	816
Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser	
260 265 270	
gtc tac tgg cac gtg att gga atg ggc acc agc ccg gaa gtg cac tcc	864
Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser	
275 280 285	
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Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala	
290 295 300	
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Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu	
305 310 315 320	
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Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His	
325 330 335	
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His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu	
340 345 350	
ccc cag ctg cgg agg aaa gct gat gaa gag gaa gat tat gat gac aat	1104
Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Glu Asp Tyr Asp Asp Asn	
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Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val	
370 375 380	
tct ccc ttt atc caa atc cgc tca gtt gcc aag aag cat cct aaa act	1200
Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr	
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Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro	
405 410 415	
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Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn	
420 425 430	
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Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met	
435 440 445	
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Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu	
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Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu	
465 470 475 480	
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Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro	
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His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys	



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aaa	tat	aaa	tgg	aca	gtg	act	gta	gaa	gat	ggg	cca	act	aaa	tca	gat	1632				
Lys	Tyr	Lys	Trp	Thr	Val	Thr	Val	Glu	Asp	Gly	Pro	Thr	Lys	Ser	Asp					
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cct	cgg	tgc	ctg	acc	cgc	tat	tac	tct	agt	ttc	gtt	aat	atg	gag	aga	1680				
Pro	Arg	Cys	Leu	Thr		Tyr	Tyr	Ser	Ser	Phe	Val	Asn	Met	Glu	Arg					
545					550					555					560					
gat	cta	gct	tca	gga	ctc	att	ggc	cct	ctc	ctc	atc	tgc	tac	aaa	gaa	1728				
Asp	Leu	Ala	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Tyr	Lys	Glu					
				565					570					575						
tct	gta	gat	caa	aga	gga	aac	cag	ata	atg	tca	gac	aag	agg	aat	gtc	1776				
Ser	Val	Asp	Gln	Arg	Gly	Asn	Gln	Ile	Met	Ser	Asp	Lys	Arg	Asn	Val					
			580					585						590						
atc	ctg	ttt	tct	gta	ttt	gat	gag	aac	cga	agc	tgg	tac	ctc	aca	gag	1824				
Ile	Leu	Phe	Ser	Val	Phe	Asp	Glu	Asn	Arg	Ser	Trp	Tyr	Leu	Thr	Glu					
		595					600					605								
aat	ata	caa	cgc	ttt	ctc	ccc	aat	cca	gct	gga	gtg	cag	ctt	gag	gat	1872				
Asn	Ile	Gln	Arg	Phe	Leu	Pro	Asn	Pro	Ala	Gly	Val	Gln	Leu	Glu	Asp					
		610				615					620									
cca	gag	ttc	caa	gcc	tcc	aac	atc	atg	cac	agc	atc	aat	ggc	tat	gtt	1920				
Pro	Glu	Phe	Gln	Ala	Ser	Asn	Ile	Met	His	Ser	Ile	Asn	Gly	Tyr	Val					
625					630				635						640					
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Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp					
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Ser	Gly	Tyr	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr					
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cta	ttc	cca	ttc	tca	gga	gaa	act	gtc	ttc	atg	tcg	atg	gaa	aac	cca	2112				
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Gly	Leu	Trp	Ile	Leu	Gly	Cys	His	Asn	Ser	Asp	Phe	Arg	Asn	Arg	Gly					
705					710					715					720					
atg	acc	gcc	tta	ctg	aag	gtt	tct	agt	tgt	gac	aag	aac	act	ggt	gat	2208				
Met	Thr	Ala	Leu	Leu	Lys	Val	Ser	Ser	Cys	Asp	Lys	Asn	Thr	Gly	Asp					
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aac	aat	gcc	att	gaa	cct	agg	agc	ttc	tcc	cag	aat	tca	aga	cac	cct	2304				
Asn	Asn	Ala	Ile	Glu	Pro	Arg	Ser	Phe	Ser	Gln	Asn	Ser	Arg	His	Pro					
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	785				790				795						800	
gat	acc	ata	tca	gtt	gaa	atg	aag	aag	gaa	gat	ttt	gac	att	tat	gat	2448
Asp	Thr	Ile	Ser	Val	Glu	Met	Lys	Lys	Glu	Asp	Phe	Asp	Ile	Tyr	Asp	
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Glu	Asp	Glu	Asn	Gln	Ser	Pro	Arg	Ser	Phe	Gln	Lys	Arg	Thr	Arg	His	
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Tyr	Phe	Ile	Ala	Ala	Val	Glu	Gln	Leu	Trp	Asp	Tyr	Gly	Met	Ser	Glu	
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Ser	Pro	Arg	Ala	Leu	Arg	Asn	Arg	Ala	Gln	Asn	Gly	Glu	Val	Pro	Arg	
	850					855					860					
ttc	aag	aag	gtg	gtc	ttc	cgg	gaa	ttt	gct	gac	ggc	tcc	ttc	acg	cag	2640
Phe	Lys	Lys	Val	Val	Phe	Arg	Glu	Phe	Ala	Asp	Gly	Ser	Phe	Thr	Gln	
	865				870				875						880	
ccg	tcg	tac	cgc	ggg	gaa	ctc	aac	aaa	cac	ttg	ggg	ctc	ttg	gga	ccc	2688
Pro	Ser	Tyr	Arg	Gly	Glu	Leu	Asn	Lys	His	Leu	Gly	Leu	Leu	Gly	Pro	
				885					890					895		
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Tyr	Ile	Arg	Ala	Glu	Val	Glu	Asp	Asn	Ile	Met	Val	Thr	Phe	Lys	Asn	
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cag	gcg	tct	cgt	ccc	tat	tcc	ttc	tac	tcg	agc	ctt	att	tct	tat	ccg	2784
Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser	Ser	Leu	Ile	Ser	Tyr	Pro	
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gat	gat	cag	gag	caa	ggg	gca	gaa	cct	cga	aaa	aac	ttt	gtc	aag	cct	2832
Asp	Asp	Gln	Glu	Gln	Gly	Ala	Glu	Pro	Arg	Lys	Asn	Phe	Val	Lys	Pro	
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Asn	Glu	Thr	Lys	Thr	Tyr	Phe	Trp	Lys	Val	Gln	His	His	Met	Ala	Pro	
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Thr	Glu	Asp	Glu	Phe	Asp	Cys	Lys	Ala	Trp	Ala	Tyr	Phe	Ser	Asp	Val	
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gac	ctg	gaa	aaa	gat	gtg	cac	tca	ggc	ttg	atc	ggc	ccc	ctt	ctg	atc	2976
Asp	Leu	Glu	Lys	Asp	Val	His	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	
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Cys	Arg	Ala	Asn	Thr	Leu	Asn	Ala	Ala	His	Gly	Arg	Gln	Val	Thr	Val	
		995					1000					1005				
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Gln	Glu	Phe	Ala	Leu	Phe	Phe	Thr	Ile	Phe	Asp	Glu	Thr	Lys	Ser	Trp	
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Gln Met Glu Asp	Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile			
	1045	1050	1055	
aat ggc tat gtg atg gat aca ctc cct ggc tta gta atg gct cag aat	3216			
Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn				
	1060	1065	1070	
caa agg atc cga tgg tat ctg ctc agc atg ggc agc aat gaa aat atc	3264			
Gln Arg Ile Arg Trp Tyr Leu Ser Met Gly Ser Asn Glu Asn Ile				
	1075	1080	1085	
cat tcg att cat ttt agc gga cac gtg ttc agt gta cgg aaa aag gag	3312			
His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu				
	1090	1095	1100	
gag tat aaa atg gcc gtg tac aat ctc tat ccg ggt gtc ttt gag aca	3360			
Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr				
	1105	1110	1115	1120
gtg gaa atg cta ccg tcc aaa gtt gga att tgg cgg aat aga tgc ctg	3408			
Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Asn Arg Cys Leu				
	1125	1130	1135	
att ggc gag cac ctg caa gct ggg atg agc acg act ttc ctg gtg tac	3456			
Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr				
	1140	1145	1150	
agc aag aag tgt cag act ccc ctg gga atg gct tct gga cac att aga	3504			
Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg				
	1155	1160	1165	
gat ttt cag att aca gct tca gga caa tat gga cag tgg gcc cca aag	3552			
Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys				
	1170	1175	1180	
ctg gcc aga ctt cat tat tcc gga tca atc aat gcc tgg agc acc aag	3600			
Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys				
	1185	1190	1195	1200
gag ccc ttt tct tgg atc aag gtg gat ctg ttg gca cca atg att att	3648			
Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile				
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cac ggc atc aag acc cag ggt gcc cgt cag aag ttc tcc agc ctc tac	3696			
His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr				
	1220	1225	1230	
atc tct cag ttt atc atc atg tat agt ctt gat ggg aag aag tgg cag	3744			
Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln				
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act tat cga gga aat tcc act gga acc tta atg gtc ttc ttt ggc aat	3792			
Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn				
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Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile				
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Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr				
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ctt cgc atg gag ttg atg ggc tgt gat tta aat agt tgc agc atg cca	3936
Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro	
1300 1305 1310	
ttg gga atg gag agt aaa gca ata tca gat gca cag att act gct tca	3984
Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser	
1315 1320 1325	
tcc tac ttt acc aat atg ttt gcc acc tgg tct cct tca aaa gct cga	4032
Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg	
1330 1335 1340	
ctt cac ctc caa ggg agg agt aat gcc tgg aga cct cag gtg aat aat	4080
Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn	
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cca aaa gag tgg ctg caa gtg gac ttc cag aag aca atg aaa gtc aca	4128
Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr	
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Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val	
1380 1385 1390	
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Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu	
1395 1400 1405	
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Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser	
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Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr	
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Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met	
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<220>

<223> HP63/OL -- factor VIII variant

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Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr	
35 40 45	
Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val	
50 55 60	
Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser	
65 70 75 80	
Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile	
85 90 95	

Gln	Ala	Glu	Val	Tyr	Asp	Thr	Val	Val	Val	Thr	Leu	Lys	Asn	Met	Ala
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Ser	His	Pro	Val	Ser	Leu	His	Ala	Val	Gly	Val	Ser	Phe	Trp	Lys	Ser
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Ser	Glu	Gly	Ala	Glu	Tyr	Glu	Asp	His	Thr	Ser	Gln	Arg	Glu	Lys	Glu
	130					135					140				
Asp	Asp	Lys	Val	Leu	Pro	Gly	Lys	Ser	Gln	Thr	Tyr	Val	Trp	Gln	Val
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Leu	Lys	Glu	Asn	Gly	Pro	Thr	Ala	Ser	Asp	Pro	Pro	Cys	Leu	Thr	Tyr
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Ser	Tyr	Leu	Ser	His	Val	Asp	Leu	Val	Lys	Asp	Leu	Asn	Ser	Gly	Leu
			180					185					190		
Ile	Gly	Ala	Leu	Leu	Val	Cys	Arg	Glu	Gly	Ser	Leu	Thr	Arg	Glu	Arg
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Thr	Gln	Asn	Leu	His	Glu	Phe	Val	Leu	Leu	Phe	Ala	Val	Phe	Asp	Glu
	210					215					220				
Gly	Lys	Ser	Trp	His	Ser	Ala	Arg	Asn	Asp	Ser	Trp	Thr	Arg	Ala	Met
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Asp	Pro	Ala	Pro	Ala	Arg	Ala	Gln	Pro	Ala	Met	His	Thr	Val	Asn	Gly
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Tyr	Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Lys	Lys	Ser
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Val	Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Ser	Pro	Glu	Val	His	Ser
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Ile	Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	His	His	Arg	Gln	Ala
	290					295					300				
Ser	Leu	Glu	Ile	Ser	Pro	Leu	Thr	Phe	Leu	Thr	Ala	Gln	Thr	Phe	Leu
305					310				315						320
Met	Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	His
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His	Gly	Gly	Met	Glu	Ala	His	Val	Arg	Val	Glu	Ser	Cys	Ala	Glu	Glu
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Pro	Gln	Leu	Arg	Arg	Lys	Ala	Asp	Glu	Glu	Glu	Asp	Tyr	Asp	Asp	Asn
	355					360						365			
Leu	Tyr	Asp	Ser	Asp	Met	Asp	Val	Val	Arg	Leu	Asp	Gly	Asp	Asp	Val
	370				375						380				
Ser	Pro	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr
385					390				395						400
Trp	Val	His	Tyr	Ile	Ala	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro
			405					410						415	
Leu	Val	Leu	Ala	Pro	Asp	Asp	Arg	Ser	Tyr	Lys	Ser	Gln	Tyr	Leu	Asn
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Asn	Gly	Pro	Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Val	Arg	Phe	Met
	435					440						445			
Ala	Tyr	Thr	Asp	Glu	Thr	Phe	Lys	Thr	Arg	Glu	Ala	Ile	Gln	His	Glu
	450					455					460				
Ser	Gly	Ile	Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	Val	Gly	Asp	Thr	Leu
465					470				475						480
Leu	Ile	Ile	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro
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His	Gly	Ile	Thr	Asp	Val	Arg	Pro	Leu	Tyr	Ser	Arg	Arg	Leu	Pro	Lys
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Gly	Val	Lys	His	Leu	Lys	Asp	Phe	Pro	Ile	Leu	Pro	Gly	Glu	Ile	Phe
	515						520					525			
Lys	Tyr	Lys	Trp	Thr	Val	Thr	Val	Glu	Asp	Gly	Pro	Thr	Lys	Ser	Asp
	530					535					540				
Pro	Arg	Cys	Leu	Thr	Arg	Tyr	Tyr	Ser	Ser	Phe	Val	Asn	Met	Glu	Arg
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Asp	Leu	Ala	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Tyr	Lys	Glu
			565					570						575	
Ser	Val	Asp	Gln	Arg	Gly	Asn	Gln	Ile	Met	Ser	Asp	Lys	Arg	Asn	Val
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Ile	Leu	Phe	Ser	Val	Phe	Asp	Glu	Asn	Arg	Ser	Trp	Tyr	Leu	Thr	Glu
	595						600					605			
Asn	Ile	Gln	Arg	Phe	Leu	Pro	Asn	Pro	Ala	Gly	Val	Gln	Leu	Glu	Asp
	610					615					620				

Pro	Glu	Phe	Gln	Ala	Ser	Asn	Ile	Met	His	Ser	Ile	Asn	Gly	Tyr	Val	625	630	635	640
Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp	645	650	655	
Tyr	Ile	Leu	Ser	Ile	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe	660	665	670	
Ser	Gly	Tyr	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr	675	680	685	
Leu	Phe	Pro	Phe	Ser	Gly	Glu	Thr	Val	Phe	Met	Ser	Met	Glu	Asn	Pro	690	695	700	
Gly	Leu	Trp	Ile	Leu	Gly	Cys	His	Asn	Ser	Asp	Phe	Arg	Asn	Arg	Gly	705	710	715	720
Met	Thr	Ala	Leu	Leu	Lys	Val	Ser	Ser	Cys	Asp	Lys	Asn	Thr	Gly	Asp	725	730	735	
Tyr	Tyr	Glu	Asp	Ser	Tyr	Glu	Asp	Ile	Ser	Ala	Tyr	Leu	Leu	Ser	Lys	740	745	750	
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Asp	Thr	Ile	Ser	Val	Glu	Met	Lys	Lys	Glu	Asp	Phe	Asp	Ile	Tyr	Asp	805	810	815	
Glu	Asp	Glu	Asn	Gln	Ser	Pro	Arg	Ser	Phe	Gln	Lys	Arg	Thr	Arg	His	820	825	830	
Tyr	Phe	Ile	Ala	Ala	Val	Glu	Gln	Leu	Trp	Asp	Tyr	Gly	Met	Ser	Glu	835	840	845	
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Phe	Lys	Lys	Val	Val	Phe	Arg	Glu	Phe	Ala	Asp	Gly	Ser	Phe	Thr	Gln	865	870	875	880
Pro	Ser	Tyr	Arg	Gly	Glu	Leu	Asn	Lys	His	Leu	Gly	Leu	Leu	Gly	Pro	885	890	895	
Tyr	Ile	Arg	Ala	Glu	Val	Glu	Asp	Asn	Ile	Met	Val	Thr	Phe	Lys	Asn	900	905	910	
Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser	Ser	Leu	Ile	Ser	Tyr	Pro	915	920	925	
Asp	Asp	Gln	Glu	Gln	Gly	Ala	Glu	Pro	Arg	Lys	Asn	Phe	Val	Lys	Pro	930	935	940	
Asn	Glu	Thr	Lys	Thr	Tyr	Phe	Trp	Lys	Val	Gln	His	His	Met	Ala	Pro	945	950	955	960
Thr	Glu	Asp	Glu	Phe	Asp	Cys	Lys	Ala	Trp	Ala	Tyr	Phe	Ser	Asp	Val	965	970	975	
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Cys	Arg	Ala	Asn	Thr	Leu	Asn	Ala	His	Gly	Arg	Gln	Val	Thr	Val		995	1000	1005	
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Gln	Met	Glu	Asp	Pro	Thr	Leu	Lys	Glu	Asn	Tyr	Arg	Phe	His	Ala	Ile	1045	1050	1055	
Asn	Gly	Tyr	Val	Met	Asp	Thr	Leu	Pro	Gly	Leu	Val	Met	Ala	Gln	Asn	1060	1065	1070	
Gln	Arg	Ile	Arg	Trp	Tyr	Leu	Leu	Ser	Met	Gly	Ser	Asn	Glu	Asn	Ile	1075	1080	1085	
His	Ser	Ile	His	Phe	Ser	Gly	His	Val	Phe	Ser	Val	Arg	Lys	Lys	Glu	1090	1095	1100	
Glu	Tyr	Lys	Met	Ala	Val	Tyr	Asn	Leu	Tyr	Pro	Gly	Val	Phe	Glu	Thr	1105	1110	1115	1120
Val	Glu	Met	Leu	Pro	Ser	Lys	Val	Gly	Ile	Trp	Arg	Asn	Arg	Cys	Leu	1125	1130	1135	
Ile	Gly	Glu	His	Leu	Gln	Ala	Gly	Met	Ser	Thr	Thr	Phe	Leu	Val	Tyr	1140	1145	1150	

Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg  
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 Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys  
 1170 1175 1180  
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 Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile  
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 1250 1255 1260  
 Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile  
 1265 1270 1275 1280  
 Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr  
 1285 1290 1295  
 Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro  
 1300 1305 1310  
 Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser  
 1315 1320 1325  
 Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg  
 1330 1335 1340  
 Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn  
 1345 1350 1355 1360  
 Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr  
 1365 1370 1375  
 Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val  
 1380 1385 1390  
 Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu  
 1395 1400 1405  
 Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser  
 1410 1415 1420  
 Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr  
 1425 1430 1435 1440  
 Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met  
 1445 1450 1455  
 Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr  
 1460 1465